


ORIGINAL ARTICLE

Antidepressant and antipsychotic prescribing in patients with type 2 diabetes in Scotland: A time-trend analysis from 2004 to 2021

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Abstract

Aims: Prescribing of antidepressant and antipsychotic drugs in general populations has increased in the United Kingdom, but prescribing trends in people with type 2 diabetes (T2D) have not previously been investigated. The aim of this study was to describe time trends in annual prevalence of antidepressant and antipsychotic drug prescribing in adult patients with T2D.

Methods: We conducted repeated annual cross-sectional analyses of a population-based diabetes registry with 99% coverage, derived from primary and secondary care data in Scotland, from 2004 to 2021. For each cross-sectional calendar year time period, we calculated the prevalence of antidepressant and antipsychotic drug prescribing, overall and by sociodemographic characteristics and drug subtype.

Results: The number of patients with a T2D diagnosis in Scotland increased from 161 915 in 2004 to 309 288 in 2021. Prevalence of antidepressant and antipsychotic prescribing in patients with T2D increased markedly between 2004 and 2021 (from 20.0 per 100 person-years to 33.3 per 100 person-years and from 2.8 per 100 person-years to 4.7 per 100 person-years, respectively). We observed this pattern for all drug subtypes except for first-generation antipsychotics, prescribing of which remained largely stable. The degree of increase, as well as the overall prevalence of prescribing, differed by age, sex, socioeconomic status and subtype of drug class.

Conclusions: There has been a marked increase in the prevalence of antidepressant and antipsychotic prescribing in patients with T2D in Scotland. Further research should identify the reasons for this increase, including indication for use and the extent to which this reflects increases in incident prescribing rather than increased duration.

KEYWORDS

antidepressant drugs; antipsychotic drugs; diabetes mellitus, type 2; prescribing trends; primary health care; Scotland

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1 | INTRODUCTION

Antidepressant and antipsychotic drugs are psychotropic medications recommended in the treatment of major depression, bipolar disorder and schizophrenia.^{1,2} They are, however, increasingly prescribed for a wider range of indications, with about one-third of antidepressants and up to two-thirds of antipsychotics prescribed for conditions such as insomnia, migraine and agitation in people with dementia.³⁻⁵ A particularly common alternative indication for antidepressant prescribing is chronic pain, including diabetic neuropathy.⁶

Prescribing of antidepressants and antipsychotics in general populations (i.e., those not defined by presence or absence of specific conditions) has increased in the United Kingdom (UK) and elsewhere in recent years.⁷⁻¹² Increased antidepressant prescribing is attributed to longer duration of use rather than increased incidence of prescribing.^{8,9} To our knowledge, no previous study has reported on time trends in antipsychotic prescribing in people with type 2 diabetes (T2D). Studies reporting on trends in antidepressant prescribing in people with T2D have focused on people with comorbid depression and have been conducted almost exclusively in the United States.¹³ It is important to investigate prescribing trends in this particular sub-population given the likely use of these drugs in people with T2D for a wider range of indications. Moreover, potential adverse effects of these medications, including weight gain,¹⁴⁻¹⁶ dyslipidaemia^{17,18} and increased risk of cerebro- and cardiovascular morbidity¹⁹⁻²¹ are particularly concerning in people with T2D.²² T2D comorbid with mental illness is also associated with poorer diabetes outcomes, including all-cause mortality, cardiovascular disease and other complications.²³⁻²⁷ The extent to which psychotropic medication, including antidepressant and antipsychotic drugs, contribute to these poorer outcomes remains under-investigated.²⁸

We therefore aimed to describe annual prevalence of antidepressant and antipsychotic drug prescribing, overall and by age, sex, socioeconomic status and drug subtype, in patients with T2D in Scotland, from 2004 to 2021.

2 | METHODS

2.1 | Population

We identified our study population from the Scottish Diabetes Research Network National Diabetes Study dataset (SDRN-NDS),²⁹ a population-based registry of 99% of patients with diabetes in Scotland. Patients are identified on the basis of diagnostic codes recorded in electronic records for clinical purposes, such as identification of people who are eligible for diabetes retinal screening. The registry integrates data related to diabetes care from primary and secondary care data sources, including demographic, clinical, biochemical and primary care prescribing information for all conditions, regardless of whether the recipient is liable for the fixed dispensing charge for non-exempt populations in the National Health Service, and is linked to

What is already known about this subject

- Whilst antidepressant and antipsychotic drug prescribing has increased in UK general populations, less is known about these prescribing trends in patients with type 2 diabetes.
- Potential adverse effects are of significant concern, particularly in patients with diabetes who may be prescribed such drugs for a wide range of indications.

What this study adds

- Antidepressant and antipsychotic prescribing prevalence increased in patients with type 2 diabetes in Scotland between 2004 and 2021.
- Degree of change differed by sociodemographic factors including age, sex and socioeconomic status.
- Further research should identify reasons for and consequences of this increase, including the contribution of increased incidence of prescribing.

other health data including hospital admission and mortality records. We included patients diagnosed with T2D aged 18 years or over on or prior to 31 December 2021.

We established annual cross-sectional time periods, from 1 January to 31 December, in the calendar years 2004 to 2021. We chose the study's start year as 2004 as this was the earliest year for which population coverage of incident and prevalent diabetes in the registry was close to complete. Patients contributed person-years to the cross-sectional time period from 1 January in the corresponding year for patients with prevalent diabetes or from date of diabetes diagnosis in that year for patients with incident diabetes. Follow-up was censored at date of death or on 31 December 2021.

2.2 | Identification of antidepressant and antipsychotic drugs

We identified antidepressant and antipsychotic drug prescribing using relevant Anatomical Therapeutic Chemical (ATC) codes from primary care data.³⁰ Antidepressants were identified as drugs with an ATC code with prefix of N06A. Antipsychotics were identified as drugs with an ATC code with prefix of N05A, excluding lithium and prochlorperazine, frequently prescribed in the United Kingdom at low doses to treat nausea and vertigo (Tables S1 and S2). For the purposes of this study, antidepressant and antipsychotic prescribing included any relevant drug, prescribed at any dose and for any length of time.

2.3 | Annual prevalence

We calculated annual crude and age- and sex-standardized prevalence of antidepressant and antipsychotic drug prescribing using the age and sex distribution of the 2004 study population as an internal standard. We described prevalence for each broad drug class stratified by age at date of entry in each year (categorized as <55, 55–64, 65–74, and ≥75 years), sex and extremes of socioeconomic status. Socioeconomic status was defined using the area-based 2016 Scottish Index of Multiple Deprivation (SIMD), based on place of residence. This comprises around 7000 small area data zones combining 38 indicators of deprivation across seven domains, including employment, income, health, education, geographic access, crime and housing.³¹ We also stratified by antidepressant and antipsychotic subtype, using non-mutually exclusive groupings where patients prescribed multiple subtypes of psychotropic drugs in any calendar year were represented in all relevant groups. We categorized antidepressant subtypes as follows: selective serotonin reuptake inhibitors (SSRIs); tricyclic antidepressants (TCAs); and ‘other antidepressants’, comprising serotonin and noradrenaline reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs) and all other antidepressants. We categorized antipsychotic subtypes as first-generation antipsychotics (FGAs) and second-generation antipsychotics (SGAs). We calculated absolute and proportional differences in prevalence of drug prescribing from 2004 to 2021. All analyses were conducted using R version 3.6.

3 | RESULTS

The number of patients with a diagnosis of T2D in Scotland increased from 161 915 in 2004 to 309 288 in 2021, with 150 784 and 295 434 person-years for each year, respectively. This was

driven by increased prevalence of T2D, with incident T2D decreasing from 10.4% to 5.3% (Tables 1 and S3). The mean age of patients increased from 64.8 to 66.6 years, whilst the proportion of males increased from 53.5% to 56.5%. However, age-sex standardized prevalence of psychotropic drug prescribing was broadly similar to crude prevalence, indicating that changes in the distribution of these characteristics had little impact on psychotropic prescribing patterns over time.

Age-sex standardized annual prevalence of antidepressant prescribing increased by 67.0%, from 20.0 per 100 person-years in 2004 to 33.3 per 100 person-years in 2021, with an annual increase observed for all years except 2020 (Table S4). This increase was observed for all subtypes of antidepressants (Figure 1; Tables S5–S7) but was largest for ‘other antidepressants’, with prescribing prevalence more than doubling between 2004 (3.9 per 100 person-years) and 2021 (10.8 per 100 person-years). Prevalence of antidepressant prescribing increased in all age groups, but both absolute and proportional increases were greatest in patients aged under 55 years and lowest in patients aged 75 and over. In 2021, antidepressant prescribing prevalence was 42.5 and 24.6 per 100 person-years for females and males, respectively. Although the prevalence of antidepressant prescribing increased in both males and females over the study period, the absolute increase was greater in females (16.6 per 100 person-years) than males (9.9 per 100 person-years). Proportional increases were similar for both sexes (64.1% and 66.7% for females and males, respectively). Antidepressant prescribing was more common in patients living in areas of highest versus lowest deprivation (40.0 and 23.9 per 100 person-years, respectively, in 2021). Absolute and proportional increases in antidepressant prescribing prevalence were greater among people living in the most compared to least deprived area and were particularly pronounced for the prescribing of ‘other antidepressants’ (Figure 2; Table S7).

TABLE 1 Characteristics of people with a diagnosis of type 2 diabetes in Scotland for selected years.

	2004	2012	2021
Total, <i>n</i>	161 915	252 000	309 288
Total person-years for each calendar year	150 784	238 194	295 434
Median (IQR) duration of diabetes (years)	4.0 (7.7)	6.2 (8.6)	8.9 (10.7)
Prevalent ^a (%)	145 056 (89.6)	233 002 (92.5)	292 891 (94.7)
Incident (%)	16 859 (10.4)	18 998 (7.5)	16 397 (5.3)
Sex (male) (%)	86 562 (53.5)	139 075 (55.2)	174 771 (56.5)
Mean (SD) age ^b (years)	64.8 (12.7)	65.6 (12.9)	66.6 (13.0)
SIMD quintile			
1 (most deprived) (%)	37 662 (24.6)	58 440 (23.9)	72 783 (23.9)
2 (%)	36 281 (23.7)	56 559 (23.1)	70 333 (23.1)
3 (%)	31 622 (20.6)	50 444 (20.6)	62 237 (20.4)
4 (%)	26 388 (17.2)	44 058 (18.0)	55 112 (18.1)
5 (least deprived) (%)	21 207 (13.8)	35 308 (14.4)	44 174 (14.3)

Abbreviations: IQR, interquartile range; SD, standard deviation; SIMD, Scottish Index of Multiple Deprivation.

^aPrevalent diabetes defined as diabetes diagnosed on or prior to the beginning of the calendar year of the cross-sectional period.

^bAt entry into relevant calendar year.

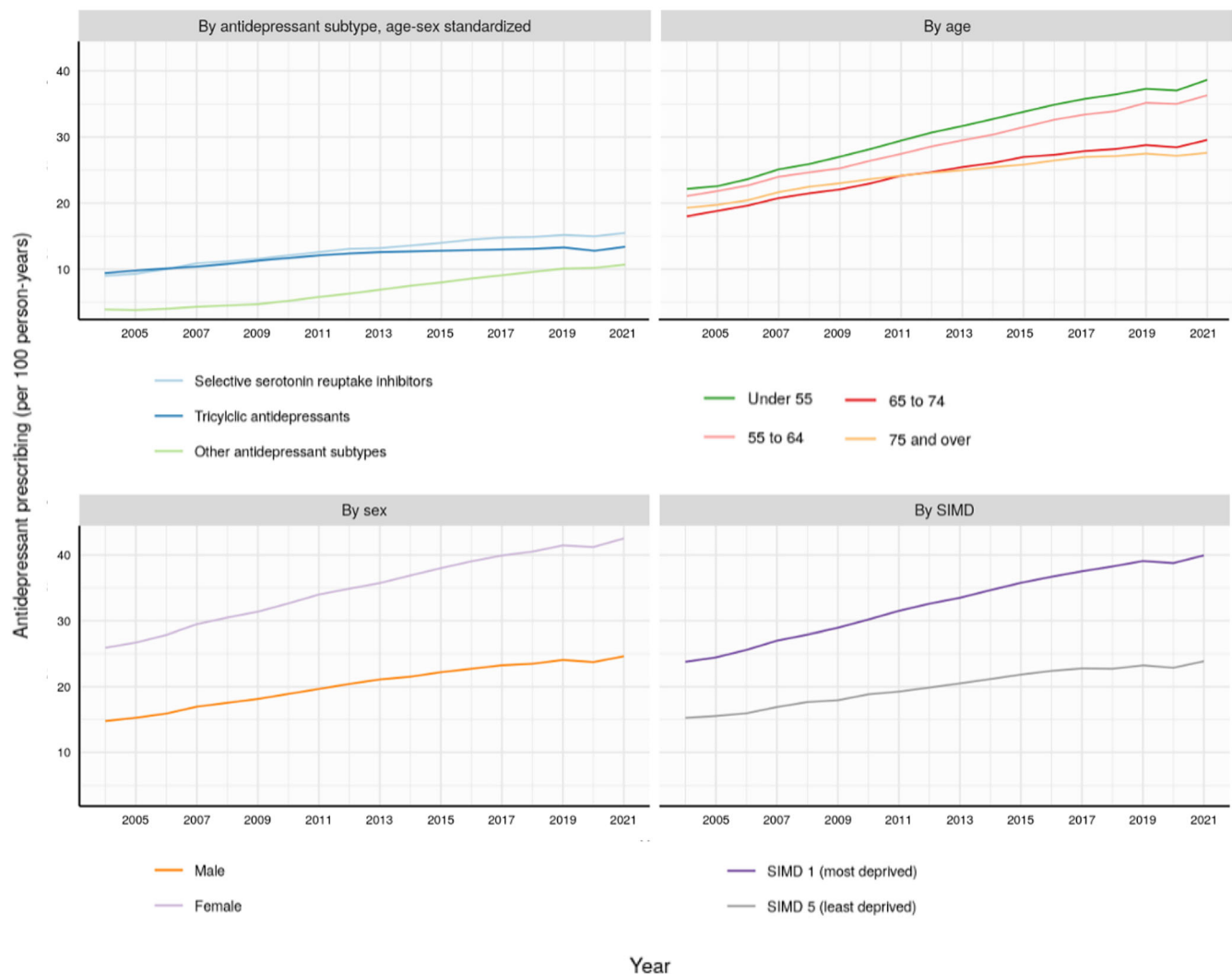


FIGURE 1 Annual prevalence of antidepressant prescribing by subtype (age-sex standardized), age, sex and Scottish Index of Multiple Deprivation (SIMD) quintile extremes, 2004–2021.

Age-sex standardized overall annual prevalence of antipsychotic prescribing increased by 69.5% over the study period, from 2.8 per 100 person-years in 2004 to 4.7 per 100 person-years in 2021 (Table S8). Prevalence of antipsychotic prescribing was consistently higher in females than males during the study period (Figure 3). In 2021, the prevalence was 5.6 and 4.0 per 100 person-years for females and males, respectively. The absolute increase in prescribing from 2004 to 2021 was similar in females (2.1 per 100 person-years) and males (1.9 per 100 person-years), although the proportional increase in prevalence was greater in males (88.6%) than females (60.3%). Antipsychotic prescribing prevalence was higher in people living in areas of highest versus lowest deprivation (5.9 and 3.5 per 100 person-years in 2021, respectively; Figure 3). Increases in antipsychotic prescribing were driven by prescribing of SGAs, which more than doubled from 1.5 per 100 person-years in 2004 to 3.3 per 100 person-years in 2021 (Table S9). This increase was observed for all age groups, but both absolute and proportional increases were greatest in patients aged <65 years (Table S9). The increase in

prescribing of SGAs was also more marked in patients living in the most compared to least deprived areas (132% and 79.3%, respectively; Figure 4; Table S9). Prescribing of FGAs remained largely stable overall, with some differences by age (Table S10). There was a 70.5% increase in FGA prescribing in patients aged ≥ 75 years, whereas for all other age categories there was either no change or a decrease in FGA prescribing. Patterns of FGA prescribing also differed by socioeconomic status, with FGA prescribing prevalence generally stable in people living in the most deprived area but increasing in the least deprived areas since 2013 (Figure 4; Table S10).

4 | DISCUSSION

Overall, prevalence of prescribing of antidepressant and antipsychotic drugs in patients with T2D in Scotland increased substantially from 2004 to 2021. This trend was generally true for all drug subtypes, except for FGAs, where prescribing prevalence was stable over time.

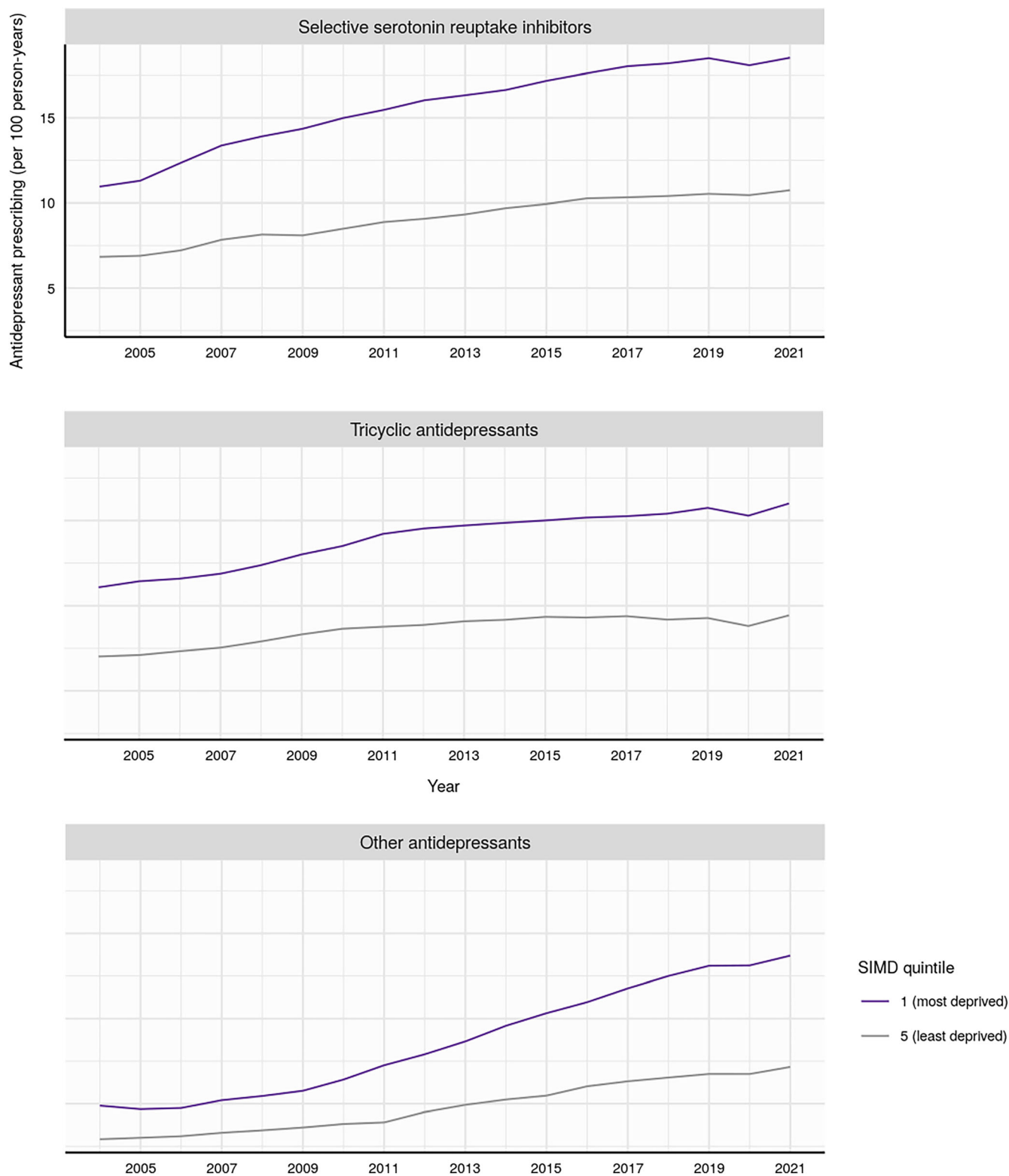


FIGURE 2 Annual prevalence of antidepressant prescribing, by Scottish Index of Multiple Deprivation (SIMD) quintile extremes, 2004–2021.

The degree of change in prevalence over time differed by sociodemographic factors including age, sex and socioeconomic status.

A key strength of this study is the use of a population-based diabetes registry, which includes almost all adults with a diagnosis of

T2D in Scotland. The large study size allowed for examination of psychotropic prescribing prevalence trends over time by sociodemographic factors as well as drug class and subtype. Other strengths include length of study period and the comprehensive routine

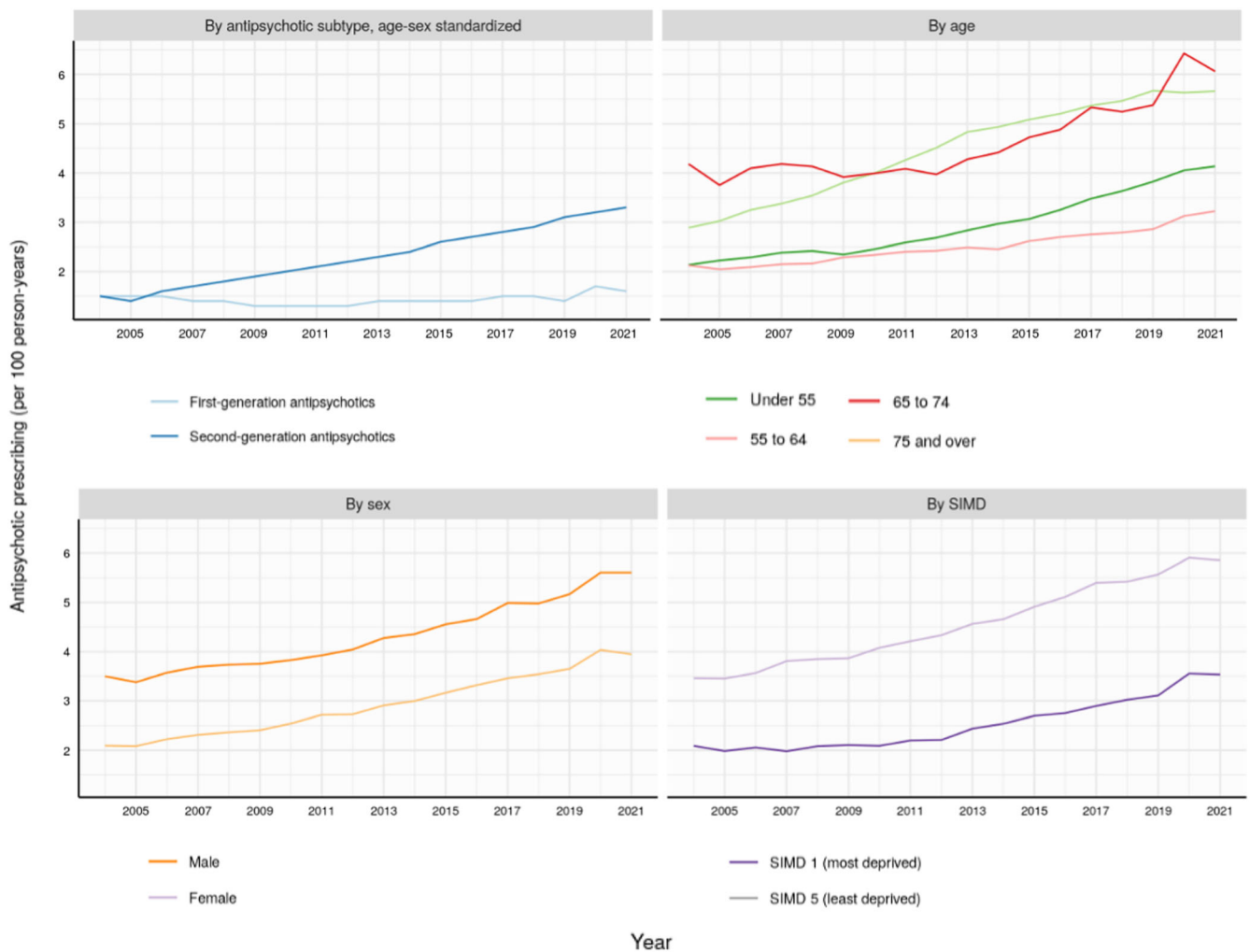


FIGURE 3 Annual prevalence of antipsychotic prescribing by subtype (age-sex standardized), age, sex and Scottish Index of Multiple Deprivation (SIMD) quintile extremes, 2004–2021.

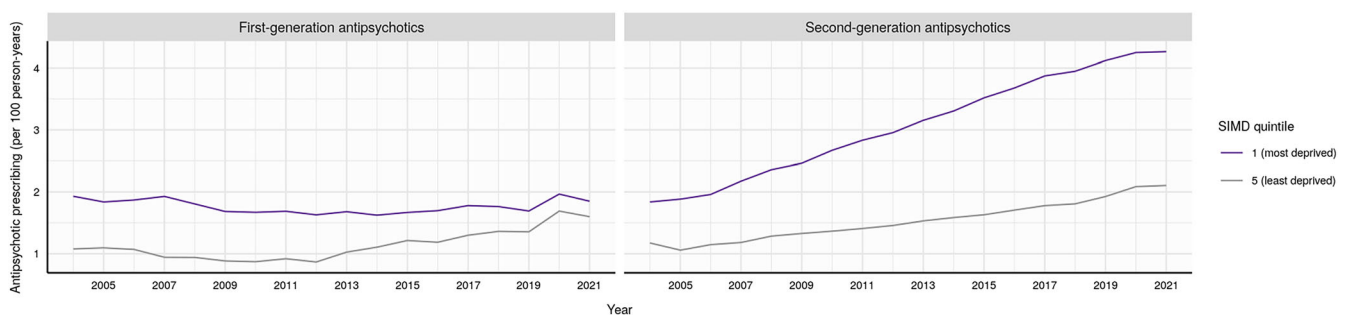


FIGURE 4 Annual prevalence of antipsychotic prescribing, by Scottish Index of Multiple Deprivation (SIMD) quintile extremes, 2004–2021.

recording of primary care prescription items. A limitation is that we did not have information on indication for prescribing. Some drugs, such as amitriptyline (a TCA), may be prescribed at lower doses for treatment of non-mental illness conditions including chronic neuropathic pain, but lack of reliable data on dose prevents us from making inferences about indications. Lack of comprehensive data on diagnoses of mental illness also limited the analysis. We did not have access

to hospital-based prescribing data. However, in the United Kingdom, drugs are routinely prescribed in the community except during periods at which patients are in receipt of inpatient care. Finally, examination of trends in incidence of prescribing was beyond the scope of this study.

The proportion of patients with T2D in Scotland prescribed antidepressant and antipsychotic drugs is approximately double the

proportion prescribed these drugs in the general population of Scotland, based on 2018–2019 data.¹¹ This is consistent with physical comorbidities being associated with antidepressant prescribing,⁸ as well as the increased risk of mental illness and neuropathic pain among patients with diabetes for which some of these drugs, including TCAs and some ‘other antidepressants’, are indicated.^{6,32,33} It may also reflect differences in sociodemographic characteristics and health service contact between the general population and patients with T2D.³⁴ As found in studies of the general population,^{7,8,10,13} prescribing prevalence in people with T2D is higher in females and people living in more deprived areas, which likely reflects the higher prevalence of some mental illnesses and of neuropathic pain in these subgroups.^{35,36}

Our finding of a substantial increase in prevalence of prescribing of antidepressant and antipsychotic medication in patients with T2D in Scotland between 2004 and 2021 aligns with prescribing trends of these psychotropic drugs in the general Scottish population.¹¹ This increased prevalence of prescribing may be due to a number of factors. Studies have suggested that the increased prescribing of antidepressants in the general population is driven by longer duration of prescribing rather than increased incidence.^{8,9,37,38} However, other studies have highlighted the increasing prescribing of antidepressants for a wider range of indications than mental illnesses,^{3,4,39} which could partly account for the trends seen in our study. Previous UK-based studies reported that increases in antidepressant prescribing in the general population in earlier decades were driven by increases in SSRI prescribing.^{7,9} In contrast, we found that the absolute and proportional increases in prescribing in the last 15 years were largest for the prescribing of ‘other antidepressants’, in keeping with findings reported for the general population of Scotland up to 2020.¹¹ One possible reason for this could be an increase in the prescribing of duloxetine, an SNRI which is used to treat both depression and neuropathic pain,⁶ and for which total prescriptions in the general population of Scotland have increased substantially in recent years.¹¹

Whilst UK studies of the general population found a decrease in prescribing of FGAs between 2007 and 2011¹⁰ and 2011 and 2016,¹² we found that prevalence of FGA prescribing remained stable overall, but increased in patients aged ≥ 75 years. This overall trend may reflect demographic differences, since patients with T2D are older on average than the general adult population.⁴⁰ A previous study also reported that FGA prescribing had increased in areas of high deprivation.¹² Interestingly, we found the opposite, with evidence of increased prevalence of FGA prescribing in patients from the least deprived group only.

Our finding that prescribing prevalence of any antidepressant subtype decreased in 2020, for all sociodemographic groups, likely reflects prescribing trends due to consequences of the COVID-19 pandemic and decreased engagement with primary care services. In contrast, we did not observe a decrease in antipsychotic prescribing in 2020. Prevalence of SGA prescribing continued to increase at a similar rate, whereas there was a sharp increase in FGA prescribing for those aged 75 years or over in particular. This may reflect lack of disruption to prescribing of antipsychotic medication for people with

severe mental illness, and an increase in treatment for dementia-related agitation in older groups. However, it is important to note that absolute numbers of FGA prescribing prevalence were small, and so prescribing trends for this particular drug subtype should be interpreted with this in mind.

The increased prevalence of psychotropic prescribing in patients with T2D is of particular concern due to a lack of understanding about potential adverse effects, including cerebro- and cardiovascular morbidity, in this population. Polypharmacy poses further challenges, as patients with T2D experience greater multimorbidity and subsequent polypharmacy associated risks compared to the general population.^{41,42} Implications include a need for clinicians to monitor for potential adverse effects in routine practice.

Future research is needed to explore the reasons for increasing prevalence of antidepressant and antipsychotic prescribing. This should include indications, appropriateness of prescribing including the role of longer term prescribing of these drugs, the mental and physical health implications for people with diabetes and clinician and patient attitudes to prescribing.

AUTHOR CONTRIBUTIONS

Charlotte R. L. Greene: Conceptualization; methodology; formal analysis; visualization; writing (original draft). **Luke A. K. Blackburn:** Data curation; writing (review and editing). **Stuart J. McGurnaghan:** Data curation; writing (review and editing). **Stewart W. Mercer:** Methodology; writing (review and editing). **Daniel J. Smith:** Methodology; supervision; writing (review and editing). **Sarah H. Wild:** Conceptualization; methodology; supervision; writing (review and editing). **Honghan Wu:** Supervision; writing (review and editing). **Caroline A. Jackson:** Conceptualization; methodology; supervision; writing (review and editing).

CONFLICT OF INTEREST STATEMENT

The authors have declared no competing interests.

DATA AVAILABILITY STATEMENT

The Scottish Diabetes Research Network epidemiology group welcomes proposals for collaborations but cannot provide access to data. Applications for data access can be made to the Public Benefit and Privacy Panel for Health and Social Care in Scotland (<https://www.informationgovernance.scot.nhs.uk/pbpphsc/>).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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