It is illegal to post this copyrighted PDF on any website. Antidepressant Prescribing in England:

Patterns and Costs

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ABSTRACT

Objective: The number of prescriptions for antidepressants (ADs) in England and Wales has almost doubled in the past decade. The objective of this article is to describe the current prescribing rates of different antidepressants by general practice (GP) practice.

Methods: We collated the prescribing behavior in each GP practice in the year April 1, 2017, to March 31, 2018. The monthly GP practice prescribing data reports for medication prescribing for each British National Formulary code and practice, as well as the prescriptions, quantity, and costs were examined in relation to prescribing practice.

Results: The data showed that 2.1 billion doses of antidepressant were prescribed to a total population of 52 million people. That equates to 11% of individuals taking \geq 1 antidepressants on any day. Selective serotonin reuptake inhibitors (SSRIs) were the most prescribed class of ADs, with sertraline the most prescribed SSRI. The other most prescribed ADs were citalopram, fluoxetine, and mirtazapine. Some older agents, such as trimipramine and doxepin, are prescribed at a very high tariff.

Conclusions: Broadly, the findings are in keeping with National Institute for Health and Care Excellence guidance in that the bulk of prescriptions were for SSRIs. Regular audit of patient treatment at a general practice level will ensure appropriate targeted use of licensed medications as supported by the evidence base.

Prim Care Companion CNS Disord 2020;22(2):19m02552

To cite: Heald AH, Stedman M, Davies M, et al. Antidepressant prescribing in England: patterns and costs. *Prim Care Companion CNS Disord*. 2020;22(2):19m02552.

To share: https://doi.org/10.4088/PCC.19m02552 © Copyright 2020 Physicians Postgraduate Press, Inc.

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*Corresponding author: Adrian H. Heald, DM, Department of Diabetes and Endocrinology, Salford Royal Hospital, Stott Lane, Salford, Greater Manchester M6 8HD, UK (adrian.heald@manchester.ac.uk). The number of prescriptions for antidepressants (ADs) in England and Wales has almost doubled in the past decade.¹ This number far exceeds projections based on increased population and a greater number of older people. Data from National Health Service (NHS) Digital show that 70.9 million prescriptions for ADs were given out in 2018, compared with 36 million in 2008.¹

In 2017, 1 in 6 adults in England were prescribed ADs.² The figures from the United Kingdom, covering the NHS as a whole, revealed a total of 7.3 million people given at least 1 AD prescription in 2017. This total included more than 70,000 people aged < 18 years. Those aged > 60 years were twice as likely as those in their twenties to be on ADs.³

Here, we describe the current prescribing rates of different antidepressants in general practice (GP) practices in England and Wales.

METHODS

We examined the way that agents licensed to treat major depressive disorder were used across GP practices in England/ Wales in the year 2017/2018 (the NHS publishes its annual data normally based on operational years, in this case from April 1, 2017, to March 31, 2018). The analysis was at a GP practice level and not at the level of individual patient data. We also looked at national prescribing trends during the years 2014–2018.

The monthly GP practice prescribing (GPPP) data reports² for each British National Formulary (BNF) code and practice, as well as the prescriptions, quantity, and costs were examined. The BNF drug name was used. The amount of active chemical in each item of the prescribed quantity was identified. Defined daily dose (DDD) was used, which is the assumed average maintenance dose per day as published by the World Health Organization,⁴ to calculate the average daily number of individuals on each therapy during the year. The cost of each agent was determined.⁵

Hospital prescribers, including home delivery, and prescribers not participating in the Quality Outcomes Framework (QOF), who have no associated population could not be captured or used within this analysis. The QOF is the system that provides incentives to family doctor practices in the United Kingdom to manage a number of long-term conditions including depression and related disorders according to nationally agreed standards. The QOF captured 99.7% of the community prescribing activity within the study periods.

We considered in detail the medication being prescribed both by quantity and costs during the study period. Prescribing

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Clinical Points

- The number of prescriptions for antidepressants has almost doubled in the last decade.
- On any day in the United Kingdom, 11% of people take an antidepressant.
- Regular audit of prescribing will ensure appropriate and proportionate use of medication as supported by the evidence base.

from 9,187 community locations in 2017-2018 are captured within these data. Of this, 7,373 practices are participants in the QOF program, and, overall, they prescribe 99.7% of prescriptions, DDD, and costs. We also evaluated the overall average cost of medication per GP practice patient, replacing the collection of different medication indicators with a single overall average cost of antidepressant medication adjusted for the size of the GP practice.

RESULTS

The findings are summarized in Tables 1 and 2. ADs are the most prescribed category of psychotropic agents. Other psychotropic agents are not included in this analysis. The sum of DDD for 2017-2018 for ADs was 2,106,221,318 DDD at a total cost of £207,495,258 (at the time the data were collected, the conversion rate from pound sterling [£] to USD [\$] was 1 to 1.288).

This compares with 71,383,947 DDD for anxiolytics at a total cost of £17,690,586. The breakdown of costs and antidepressant use is shown in Figure 1. The inner ring shows the split of usage by dose, with the outer ring showing split by cost both for overall class and specific agents.

In GP practices in England/Wales during the 4 years from 2014-2015 to 2017-2018, there was a 37% increase in the number of people recorded on the depression register and a 22% increase in total doses of ADs. Total costs of ADs fell of different unique ADs at different dose levels increased from 94 to 107.

The average AD prescribing rate (ADPR; DDD of AD/head population/d) was 0.10, and 90% of practices fell between 0.04 and 0.16 ADPR. This equates to 10% of individuals taking an antidepressant on any day.

Selective Serotonin Reuptake Inhibitors

Selective serotonin reuptake inhibitors (SSRIs) were the most prescribed class of ADs, with sertraline the most prescribed SSRI. We found that 631,539,864 DDDs of sertraline were prescribed at a cost of £15,753,591, which equates to £0.02 per DDD. The next most prescribed SSRIs were citalopram at 459,884,804 DDDs and fluoxetine at 309,888,530 DDDs. A small amount of fluvoxamine is still prescribed at 812,944 DDDs at a cost of £0.67 per DDD.

Other Antidepressants

Large amounts of mirtazapine (189,700,638 DDDs) and venlafaxine (149,912,532 DDDs) were prescribed. The cost of venlafaxine at £0.21 remains higher than mirtazapine at £0.08, as does the cost of duloxetine at £0.27. Small amounts of agomelatine, reboxetine, and vortioxetine were prescribed. These are relatively high-cost agents at up to £0.99 in the case of agomelatine, for which 706 DDDs were prescribed at a cost of £702,000.

Tricyclics and Related Antidepressants

Amitriptyline at 157,516,372 DDDs and £0.16 per DDD was by far the most prescribed of this class of antidepressant. Lower amounts of clomipramine, imipramine, and nortriptyline are prescribed, but these medications are also used for other indications such as phobic and obsessional states in the case of clomipramine and neuropathic pain in the case of nortriptyline and amitriptyline.

Some older agents are still prescribed at a very high tariff such as trimipramine (£24.83 per DDD) and doxepin (£11.42 per DDD).

Table 1. Breakdown of Antidepressant Prescribing by Type for 2017–2018											
					% of		% of	Total	% of Total		
	GP	% of			Total		Total	Annual	Annual	Annual	DDD/
Type ^a	Practices ^b	Total	Variants ^c	ltems ^d	Items	DDD ^e	DDD	Costs	Costs ^f	Costs/DDD ^g	ltem ^h
Selective serotonin reuptake inhibitors	7,372	100	34	36,519	54	1,495,815	71	£57,527	28	£0.04	41
Other antidepressant drugs	7,368	100	26	14,781	22	400,785	19	£64,031	31	£0.16	27
Tricyclic and related antidepressant drugs	7,368	100	42	16,551	24	208,257	10	£80,851	39	£0.39	13
Monoamine oxidase inhibitors	2,713	37	5	41	0	1,526	0	£5,087	2	£3.33	37
Total	7,374	100	107	67,892	100	2,106,383	100	£207,495	100	£0.10	31

^aAs split within the British National Formulary.

^bNumber of general practice (GP) practices prescribing that medication.

^cNumber of different agents, dose levels, and formulations.

^dNumber of prescriptions.

eTotal defined daily doses (DDD) in the year.

^fAt the time the data were collected, the conversion rate from pound sterling (£) to USD (\$) was 1 to 1.288. ^gAverage costs/DDD.

^hAverage number of DDDs/prescription.

It is illegal to post this copyrighted PDF on any web Table 2. Breakdown of Each Antidepressant Type by Medication for 2017–2018

	6.0	<i></i>			o. (Total				
Tunol and Modication	GP Practices ^b	% of Total	Variants ^c	ltoma	% of	DDD ^e	% of	Annual Cost ^f	% of	Costs/ DDD ^g	DDD/ Item ^h	Patients Practice
Type ^a and Medication		TOLAI	Variants	Items	Туре	DDD*	Туре	Cost	Туре	DDD®	nem	Plactic
Selective serotonin reuptake inhil												
Sertraline	7,370	100	9	13,246	36	631,540	42	£15,754	27	£0.02	48	235
Citalopram	7,369	100	6	14,286	39	459,885	31	£23,289	40	£0.05	32	171
Fluoxetine	7,363	100	7	6,582	18	309,889	21	£11,654	20	£0.04	47	115
Paroxetine	7,307	99	6	1,369	4	54,346	4	£4,459	8	£0.08	40	20
Escitalopram	7,128	97	4	1,014	3	39,343	3	£1,871	3	£0.05	39	15
Fluvoxamine	1,813	25	2	22	0.1	813	0.1	£500	1	£0.61	37	1
Other antidepressant drugs												
Mirtazapine	7,364	100	5	8,305	56	189,701	47	£16,040	25	£0.08	23	71
Venlafaxine	7,350	100	6	4,160	28	149,913	37	£30,862	48	£0.21	36	56
Duloxetine	7,296	99	2	2,087	14	54,032	13	£14,550	23	£0.27	26	20
Flupentixol	4,285	58	2	137	1	4,488	1	£374	1	£0.08	33	3
Vortioxetine	2,572	35	3	46	0.3	1,216	0.3	£980	1.5	£0.81	26	1
Reboxetine	2,091	28	1	27	0.2	715	0.2	£419	0.7	£0.59	26	1
Agomelatine	1,437	19	1	18	0.1	706	0.2	£702	1.1	£0.99	39	1
Tryptophan	41	1	2	0	0.0	10	0.0	£16	0.0	£1.73	40	1
Nefazodone	19	0	2	0	0.0	4	0.0	£86	0.1	£19.60	32	1
Oxitriptan	4	0	2	0	0.0	2	0.0	£1	0.0	£0.65	80	1
Tricyclic and related antidepressa	nt drugs											
Amitriptyline	7,368	100	6	13,299	80	157,516	76	£25,179	31	£0.16	12	59
Trazodone	6,871	93	4	1,131	7	13,117	6	£20,754	26	£1.58	12	5
Dosulepin	6,938	94	5	790	5	11,986	6	£1,739	2	£0.15	15	5
Lofepramine	5,552	75	2	209	1	8,101	4	£2,110	3	£0.26	39	4
Nortriptyline	7,084	96	5	590	4	7,682	4	£7,438	9	£0.97	13	3
Clomipramine	6,196	84	5	296	2	6,062	3	£1,073	1	£0.18	20	3
Imipramine	5,326	72	4	154	1	2,583	1	£400	0	£0.16	17	1
Trimipramine	2,591	35	4	48	0.3	672	0.3	£16,681	20.6	£24.83	14	1
Doxepin	2,102	29	4	29	0.2	472	0.2	£5,388	6.7	£11.42	16	1
Mianserin	402	5	2	4	0.0	67	0.0	£84	0.1	£1.26	18	0
Amoxapine	1	0	1	0	0.0	1	0.0	£3	0.0	£6.26	105	1
Monoamine oxidase inhibitors												
Moclobemide	1,422	19	2	18	44	652	43	£615	12	£0.94	36	1
Tranylcypromine	574	8	1	6	16	483	32	£3,794	75	£7.85	75	2
Phenelzine	1,261	17	1	15	36	311	20	£261	5	£0.84	21	1
Isocarboxazid	171	2	1	2	4	79	5	£416	8	£5.28	46	1

^aAs split within the British National Formulary.

^bNumber of general practice (GP) practices prescribing that medication.

^cNumber of different agents, dose levels and formulations.

^dNumber of prescriptions.

^eTotal defined daily doses (DDD) in the year.

^fAt the time the data were collected, the conversion rate from pound sterling (£) to USD (\$) was 1 to 1.288.

^gAverage costs/DDD.

^hAverage number of defined daily doses/prescription.

Total defined daily doses/365/number practices prescribing that medication.

Monoamine Oxidase Inhibitors

Small amounts of the monoamine oxidase inhibitors moclobemide, tranylcypromine, and phenelzine are prescribed. These prescriptions are usually for treatment-resistant/atypical depression,⁶ and in our experience in the United Kingdom, are typically done in collaboration with a specialist psychiatry service.

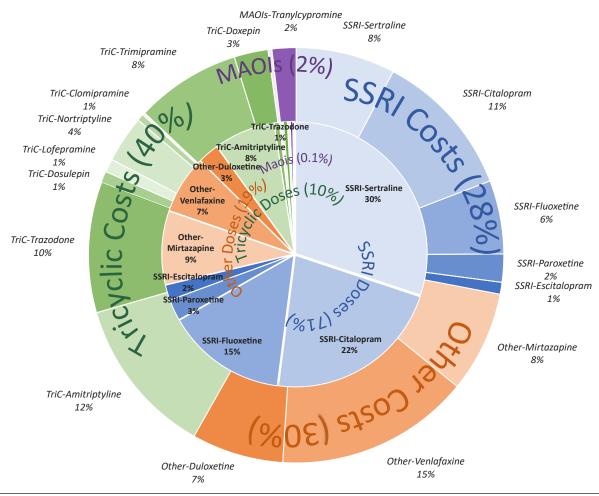
DISCUSSION

The pattern of antidepressant prescribing sits in parallel to the findings of 2 meta-analyses by Furukawa et al⁷ and Linde et al⁸ in that sertraline and citalopram, which are well tolerated, are also effective. However, agomelatine is minimally prescribed, although well tolerated and efficacious. The low prescribing rate of agomelatine may well relate to its cost at £0.99 per DDD. Furthermore, a very common use of doxepin and trazodone is for sleep.

The escalating prescription rate for ADs in the United Kingdom is cause for much debate in the public domain and among health care professionals. Our analysis is the first to look at the rates of prescribing at a GP practice level. The high volume of prescribing of sertraline in 2017–2018 may well relate to the influence of earlier research on acceptability versus efficacy of antidepressant medication.⁶

Using national GP practice–level data, we recently described how the empowerment of individuals in managing long-term conditions has the potential to reduce GP practice level prescribing of ADs.⁹ Practices that are more effective in empowering their patients, as assessed by "How confident are you in the management of your condition," prescribed fewer antidepressants. The difference Heald et al It is illegal to post this copyrighted PDF on any website

Figure 1. Breakdown by Class and Medicine of Total Annual Use (£2.1 Billion DDD≈5.8 Million Annualized Doses) and Annual Costs (£200 Million)^a



^aAt the time the data were collected, the conversion rate from pound sterling (£) to USD (\$) was 1 to 1.288. Abbreviations: SSRI = selective serotonin reuptake inhibitor, TriC = tricyclic.

between the lowest and highest decile of prescribing for this response was over 10% and is therefore potentially modifiable by changing the GP practice approach to patient empowerment. This analysis is an opportunity to review AD prescribing in each GP practice and has implications for clinical behavior and medication management.

The limitations of our analysis are that it does not look at individual patient data. Also, we were unable to differentiate between prescriptions to treat depression and other indications for antidepressants such as the use of citalopram in panic disorder, the use of fluoxetine in bulimia nervosa and obsessive-compulsive disorder, and the use of amitriptyline, nortriptyline, and duloxetine to treat neuropathic pain. However, the data cover all GP surgeries in England and Wales and thus are representative of the rates of antidepressant prescribing across these nations.

CONCLUSION

The results describe prescribing patterns in 2017–2018. Antidepressants are used across the world to treat

depression. Regular audit of patient treatment at a general practice level should facilitate appropriate targeted use of licensed medications and the cessation of medication when no longer needed. This principle applies to all prescribers of antidepressants worldwide.

Submitted: September 29, 2019; accepted December 30, 2019. Published online: April 16, 2020.

Author contributions: Drs Heald and Stedman conceived the study. Drs Heald, Stedman, and Davies conducted the data analysis. Drs Heald, Stedman, Davies, Livingston, Taylor, and Gadsby contributed to the writing of the paper. Drs Taylor and Gadsby provided an overview of the manuscript prior to submission.

Potential conflicts of interest: None.

Funding/support: None.

Ethics: As publicly available and GP-level data were used, with no individual patient data, ethics approval was not required for this study.

Data availability: Any requests for data extracts will be considered by Dr Heald as the corresponding author.

REFERENCES

1. lacobucci G. NHS prescribed record number of antidepressants last year. *BMJ*. 2019;364:1508. 2. GP Practice Prescribing Presentation-Level Data. NHS Digital. https://digital.nhs.uk/ 8. Li

catalogue. Accessed July 23, 2019. 3. Mahase E. Antidepressant prescriptions

- Manase E. Antidepressant prescriptions increased by half a million last year. Pulse website. http://www.pulsetoday.co.uk/clinical/ clinical-specialties/prescribing/antidepressantprescriptions-increased-by-half-a-million-lastyear/20037121.article. Accessed July 28, 2019.
- ATC/DDD Index 2020. WHO website. https:// www.whocc.no/atc_ddd_index/. Accessed July 23, 2019.
- 5. Prescription cost analysis: England 2018. NHS

and-information/publications/statistical/ prescription-cost-analysis/2018. Accessed July 28, 2019.

- National Institute for Health and Care Excellence website. https://cks.nice.org.uk/ depression/. Accessed July 24, 2018 and July 23, 2019.
- Furukawa TA, Salanti G, Atkinson LZ, et al. Comparative efficacy and acceptability of first-generation and second-generation antidepressants in the acute treatment of major depression: protocol for a network
- meta-analysis. *BMJ Open*. 2016;6(7):e010919.
 Linde K, Kriston L, Rücker G, et al. Efficacy and acceptability of pharmacological treatments for depressive disorders in primary care: systematic review and network meta-analysis. *Ann Fam Med*. 2015;13(1):69–79.
- Heald AH, Stedman M, Davies M, et al. Quantifying the impact of patient-practice relationship quality on the levels of the average annual antidepressant practice prescribing rate in primary care in England. *Prim Care Companion CNS Disord*. 2020;22(1):19m02528.