Research Article

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Ongoing initiatives within the Scottish National Health Service to affect the prescribing of selective serotonin reuptake inhibitors and their influence

Brian Godman*[,1,2,3], Amanj Kurdi[1,4], Holly McCabe[5], Chris F Johnson[6], Corrado Barbui[7], Sean MacBride-Stewart[6], Simon Hurding[8], Axel Leporowski[5], Marion Bennie[1] & Alec Morton[5]

[1]Strathclyde Institute of Pharmacy & Biomedicial Sciences, University of Strathclyde, Glasgow, UK
[2]Division of Clinical Pharmacology, Karolinska, Karolinska Institutet, Stockholm, Sweden
[3]Department of Public Health Pharmacy & Management, School of Pharmacy, Sefako Makgatho Health Sciences University, Garankuwa, South Africa
[4]Department of Pharmacology, College of Pharmacy, Hawler Medical University, Erbil, Iraq
[5]Department of Management Science, Strathclyde Business School, University of Strathclyde, Glasgow, UK
[6]Prescribing Support Unit, National Health Service Greater Glasgow & Clyde (NHS GGC), Glasgow, UK
[7]WHO Collaborating Centre for Research & Training in Mental Health & Service Evaluation, Department of Neuroscience, Biomedicine & Movement Sciences, Section of Psychiatry, University of Verona, Italy
[8]Therapeutics Branch, Scottish Government, Edinburgh, UK
*Author for correspondence: Tel.: +44 141 548 3825; Fax: +44 141 552 2562; brian.godman@strath.ac.uk

Aim: Increasing use of selective serotonin-reuptake inhibitors (SSRIs) in Scotland, coupled with safety concerns with some SSRIs, and the increasing availability of generic SSRIs, have resulted in multiple initiatives to improve the quality and efficiency of their prescribing in Scotland. Our aim is to assess their influence to provide future direction. **Materials & methods:** The prescription costs analysis database was used to document utilization and expenditure on SSRIs between 2001 and 2017 alongside documenting the initiatives. **Results:** Multiple interventions over the years increased international nonproprietary name prescribing up to 99.9% lowering overall costs. This, coupled with initiatives to limit escitalopram prescribing due to concerns with its value, resulted in a 73.7% reduction in SSRI expenditure between 2001 and 2017 despite a 2.34-fold increase in utilization. Safety warnings resulted in a significant reduction in the prescribing of paroxetine, citalopram and escitalopram alongside a significant increase in sertraline **Conclusion:** Multiple initiatives have increased the quality and efficiency of SSRI prescribing in Scotland providing direction to others.

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Across countries, there has been considerable growth in the use of medicines. In part, this has been driven by aging populations, an increase in primary prevention strategies, as well as single disease model guidelines and policies [1,2]. We have also seen the continual launch of new high-priced medicines [2,3]. These factors combined are adding to resource pressures within countries resulting in models and initiatives to address this [2–5]. Scotland is no exception, and during the last 20 years or more there have been multiple initiatives to enhance the quality and efficiency of prescribing to help improve patient outcomes within finite resources, providing direction to other countries.

Initiatives include encouraging high rates of international nonproprietary name (INN) prescribing with generics typically seen as similar to the originator in all but a minority of situations [6–8]. This is important as there are still concerns with generics across a number of countries [9–11]. Savings once generics become available in Scotland are enhanced by their reduced costs, which can be as low as 3% of prepatent loss originator prices [12,13]. INN prescribing is important in Scotland as pharmacists are not currently allowed to switch an originator or branded product to a generic if the physician prescribes the originator or branded product [7,14,15]. Alongside this, there have

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also been initiatives to increase the prescribing of multiple sourced products (generics) versus on-patent products in a class or related class where this does not compromise care to further save on costs. Classes include the proton pump inhibitors (PPIs), renin–angiotensin receptor blockers and statins [12,13,15].

Concomitant with this, there have also been multiple measures in Scotland to improve the quality of prescribing. These include encouraging physicians to prescribe higher doses of statins to improve long-term outcomes as well as initiatives to reduce the prescribing of lipid-lowering agents where there have been concerns with their effectiveness [12,15]. There have also been national and regional initiatives in Scotland to reduce the doses of PPIs prescribed, as well as encourage regular monitoring of patients on long-term PPIs, due to concerns with the consequences of their long-term use [16–19].

Depression and other mental health conditions, such as anxiety disorders, are prevalent in Scotland with 11.3% of the adult population in 2010–2011 prescribed antidepressants [20]. These high rates of prescribing are possibly influenced by westernized societies' expectations of happiness, and consequential medicalization of unhappiness [21,22], as well as expansion of the indications for antidepressants. The selective serotonin-reuptake inhibitors (SSRIs) are the most frequently prescribed antidepressants in Scotland, accounting for over 50% of all antidepressants prescribed in recent years [20,23,24]. However, unlike the PPIs, renin–angiotensin blockers and statins, the situation with antidepressants is more challenging as they are not readily interchangeable, which limits the potential for therapeutic switching within a class [12,13,15,25,26]. This is because antidepressants such as the SSRIs exhibit subtle differences, which can affect both their efficacy and side effects [27–29]. Having said this, there have been activities among the Health Boards (regions) in Scotland to limit the prescribing of escitalopram versus other SSRIs, including fluoxetine and citalopram, where there have been considerable differences in costs but limited differences in patient outcomes [17,30–32]. Health Board activities included prescribing targets for escitalopram [33]. They also include switching suitable patients prescribed escitalopram prior to citalopram to now being prescribed citalopram (C Johnson, P.C.). Encouragingly, 90% of patients remained on citalopram after the switch at a 3-month review. Such activities are important from a health policy perspective as they help to conserve resources without compromising care.

We have also seen initiatives in other countries to influence the prescribing of antidepressants where there have been concerns. This includes instigating prescribing restrictions for duloxetine in the management of patients with depression in Sweden due to concerns with its effectiveness and costs versus other antidepressants [34], as well as education and other activities to limit the prescribing of vortioxetine again due to concerns with its cost–effectiveness [35,36]. Such activities are likely to continue.

We are also aware that there have been concerns with the increased risk of suicides with paroxetine as well as other SSRIs since the early 2000s [37–42]. In addition, paroxetine is associated with a higher incidence of discontinuation symptoms versus other SSRIs, which necessitates a longer period of dose reduction [43]. There have also been concerns with potential QTc interval prolongation and Torsade de Pointes with citalopram and escitalopram from 2011 onward [44], although the latter may be infrequently reported [45]. The concerns with possible QTc interval prolongation with citalopram and escitalopram resulted in the MHRA in the UK and Health Boards in Scotland providing guidance on their use [46–69]. This included recommending alternative SSRIs for new patients, as well as for patients where there were concerns with citalopram and escitalopram. Alternatives included sertraline with evidence of potential improved effectiveness and safety versus other SSRIs [48,50,51]. We are also aware that Health Boards in Scotland have also assessed factors associated with higher doses of SSRIs being prescribed [20,52]. Available evidence does not support the routine prescribing of higher doses of SSRIs for the treatment of depression as this is known to increase anxiety, agitation and insomnia [53].

As a result of multiple activities in Scotland, rates of INN prescribing for the SSRIs were as high as 98–99% of their total utilization in 2007 [13]. This coupled with initiatives to limit the prescribing of escitalopram versus citalopram resulted in expenditure on the SSRIs falling in Scotland by 59% between 2001 and 2007 despite a 2.37-fold increase in their utilization [13]. This compares with appreciably increased expenditure for the SSRIs in Ireland (72% higher) and Portugal (93% higher) in 2008 and 2007 versus 2001 respectively where there were limited measures in both these countries to encourage the prescribing of lower cost multiple sourced SSRIs (generics) versus originators as well as on-patent escitalopram [13,54]. Such activities are important among high income countries with universal healthcare systems due to the continuous growth in the prescribing of medicines for patients with noncommunicable diseases including patients with depression resulting in constant financial pressures, which is enhanced by the continual launch of new premium priced medicines to address areas of unmet need [2,4,6,54-56]. Obtaining low prices for good quality generics, and promoting their use, is also very important in low and middle

income countries where access to medicines can be an issue with high patient copayment levels [57,58]. Without such considerations, illness among family members can be potentially catastrophic for them [58,59]. Currently, fluoxetine is included in the WHO list of essential medicines [60].

Consequently, the objectives of this paper are multiple. First, to assess the influence of the various multiple measures in Scotland on the overall volume and expenditure on the SSRIs in recent years, building on the earlier analysis [13]. Second, assess the extent of INN prescribing as well as the extent of price reductions for SSRIs following generic availability to help fund increased prescribing volumes without increasing costs, again building on the earlier analysis [13]. Third, assess the extent of changes in the utilization of citalopram, escitalopram, paroxetine and sertraline in recent years as a result of multiple initiatives and safety warnings. The findings will help guide future activities in Scotland as well as other countries, as all countries are looking to improve the quality and efficiency of their prescribing due to continuing pressures on resources.

We are also aware that there is a growing requirement for research evidence to guide future activities and initiatives to improve the selection, affordability and rationality of prescribing of medicines for patients with mental disorders, which can be considered as public health psychopharmacology [61]. We hope our findings help to start addressing this deficit.

Methodology

Utilization & expenditure data

We used the prescription costs analysis (PCA) data in Scotland to analyze utilization and expenditure data in ambulatory care [62]. The PCA data is compiled by the Information Services Division of NHS Scotland, which is an open source dataset collecting data on the utilization and expenditure of medicines dispensed in community pharmacies in Scotland. The NHS in Scotland is a tax payer funded, free at point of access, health service, with currently no copayment for medicines.

Information extracted from the PCA for each SSRI (N06AB – [63]) between 2001 and 2017 included: their generic name, commercial name(s), formulation(s), drug strength(s), number of dispensed units, cost per unit and total expenditure. The costs are in pounds sterling (GB£s) and include the gross ingredient costs and cost per item for all SSRIs medicines dispensed during this period. No adjustment for inflation for prices was made, which is in line with previous studies, typically due to the rapid reduction in prices in the UK once originators become available as generics [12,13,64].

While we are aware NHS Scotland routinely uses defined daily doses (DDDs) when presenting and discussing utilization data in line with international guidance [23,63,65], especially when different strengths are available such as citalopram (10, 20 and 40 mg) and sertraline (50 and 100 mg), we used items dispensed as we wanted to track this to reflect individual prescriptions, especially following changes in prescribing guidance, similar to the situation with lipid-lowering agents and PPIs [15,19]. In the case of patients with chronic diseases such as depression, a prescription in terms of 'items dispensed' is usually for 28 or 56 days. However, as previously identified, there can be a tendency in recent years for physicians to increase the length of a prescription to help with their growing workloads [15].

Demand-side measures

As before, ongoing activities within the Health Boards and NHS Scotland to encourage INN prescribing as well as selected SSRIs have been collated using the 4E methodology: Education, Engineering, Economics and Enforcement [12,13,15,66]. Education refers to initiatives such as prescribing guidance and guidelines; engineering refers to organizational or managerial interventions such as prescribing targets; economics to financial incentives such as prescribing incentive schemes; and enforcement refers to regulations from health authorities [13,15,66]. However, the latter is rare in Scotland with no actual enforcement of regulations as seen for instance in Sweden with compulsory generic substitution and prescribing restrictions for statins in Finland and Norway following generic simvastatin [67–69].

We did not typically undertake any time-series analyses as multiple interventions with interlinked activities were undertaken at different times both nationally and regionally between 2001 and 2017. However, we did undertake such a time-series analysis comparing the changes in the items dispensed for citalopram and escitalopram before and after the warnings regarding possible QTc interval prolongation and any subsequent influence on the utilization of recommended SSRIs such as sertraline [70]. A p-value > 0.05 was seen as significant.

Table 1. Selective serotonin reuptake inhibitors and their patent expiration date in Scotland from 2001 to 2017.

Generic name	Commercial name (originator)	ATC code	Year of patent expiration
Fluvoxamine	Faverin®	N06AB08	Prior to 2000
Fluoxetine	Prozac®	N06AB03	2000
Paroxetine	Seroxat®	N06AB05	Prior to 2000
Citalopram	Cipramil®	N06AB04	2002
Sertraline	Lustral®	N06AB06	2005
Escitalopram	Cipralex®	N06AB10	2014

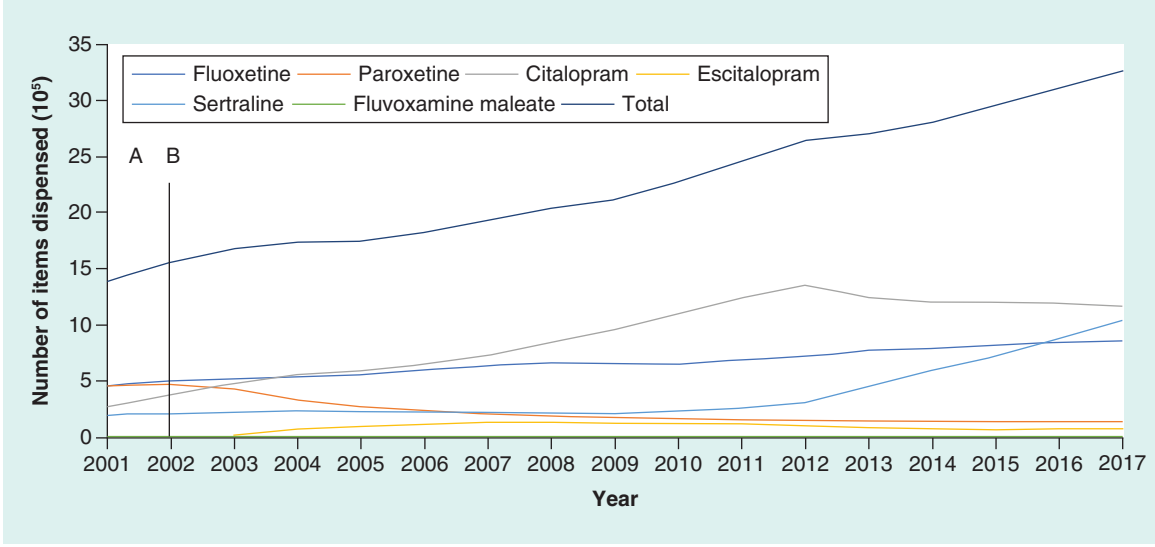

Figure 1. Selective serotonin-reuptake inhibitor utilization (items dispensed) in Scotland 2001–2017.

Results

Generic availability of SSRIs

Table 1 contains details of the year of patent expiry of the different SSRIs in Scotland.

Influence of multiple measures

A number of demand-side measures have been introduced nationally and regionally in Scotland in recent years to enhance INN prescribing as well as influence the prescribing of different SSRIs due either to concerns with their safety or value [13,17,30,31,33,40,46,48,49,51,52,71–76]. These are summarized in Table 2.

Total utilization & expenditure

There was a steady increase in the number of total SSRI items dispensed between 2001 and 2017 (Figure 1).

A total of 1.393 million items were dispensed in 2001 with a cost of GB£28.937 million, rising to 3.258 million items dispensed in 2017 at a cost of GB£7.613 million. This represents a 2.34-fold increase in SSRI utilization during this period but a 73.7% reduction in expenditure.

The increase in SSRI utilization during this period has been predominantly driven by increasing utilization of citalopram, initially rising from 19.8% of total SSRI items dispensed in 2001 (276 thousand items) to 51.3% in 2012 (1.352 million items) before falling to 35.6% in 2017 following concerns with QT prolongation (Table 2). During this period, sertraline utilization rose appreciably from 10.32% of total SSRI utilization in 2011 to 31.8% in 2017. Concurrent with this, fluoxetine utilization fell gradually from 33.2% of total SSRI items dispensed in 2001 to 26.3% in 2017 (Figure 1). The utilization of paroxetine fell steadily throughout the study period from 32.7% of total utilization in 2001 to 4.1% in 2017 following safety and other concerns, although these were not exclusively attributable to paroxetine. Overall during the study period, the number of items of paroxetine dispensed

Table 2. Summary of principal demand-side measures introduced in Scotland between 2001 and 2017 that influenced selective serotonin reuptake inhibitors utilization patterns.

Measure	Year	National or regional	Initiative
Education	2001–2017	National and regional	• Physicians typically trained in medical school to prescribe by INN name with subsequent activities in GP practices coupled with IT systems to enhance INN prescribing
	2003	National	• National warning regarding paroxetine in children
	2003	Regional (Lothian)	• Lothian highlighting the extent of savings from the prescribing of generic paroxetine vs originator
	2006	Regional (GGC)	• Fluoxetine and citalopram recommended SSRIs on the formulary list
	2008 onward	Regional (GGC)	• Educating GPs to regularly review patients on long-term antidepressants (doses prescribed, effectiveness, treatment duration, guideline improvements and costs)
	2009	Regional (GGC)	• Fluoxetine and citalopram recommended SSRIs on the formulary list
	2010	Regional (GGC)	• Sertraline added to the recommended formulary list of SSRIs
	2009/10– 2015	Regional (GGC)	• Review of patients receiving the same antidepressant for ≥2 years conducted among 180 GP practices involving >8000 patients, the majority of whom receive SSRIs
	2011	National	• MHRA warning on QT interval prolongation with citalopram and escitalopram
	2012 and 2015	Regional (GGC)	• Escitalopram and citalopram at high risk of QT prolongation
	2012	Regional (Tayside)	• Warnings of QT interval prolongation with citalopram and escitalopram
	2013	Regional (Lothian)	• Guidance on potential risks associated with the prolongation of QTc interval with different psychotropic medicines
	2017	NHS Grampian	• Fluoxetine and sertraline recommended SSRIs with sertraline recommended in patients with cardiovascular disease (caution with citalopram)
Engineering	2002	National	• Audit Scotland benchmarking DDDs of non-fluoxetine SSRIs and the extent of INN prescribing across Scotland
	2007	National	• Health improvement, Efficiency, Governance, Access to services and Treatment (HEAT) targets. NHS Boards to reduce the annual rate of increase of defined daily dose per capita of antidepressants to zero by 2009/10 and put in place the required support framework to achieve a 10% reduction in future years
	2007/2008	Regional (Lothian)	• Total number of prescribed items of escitalopram ≤10% of all SSRIs (also linked with financial incentive schemes – Economics)
	2008/09– 2012/13	Regional (GGC)	• Fluoxetine and citalopram as a % of all SSRIs, duloxetine, mirtazapine, reboxetine and venlafaxine items ≥65% (or an absolute increase of 5%) items and linked with prescribing financial incentives (Economics)
	2009/10	Regional (GGC)	• Escitalopram prescribing <5% of all SSRIs items and linked to prescribing financial incentives (Economics) • Fluoxetine 60 mg capsules to 3 × 20 mg capsules (GB£39/patient as opposed to GB£360/patient) and linked to prescribing financial incentives (Economics)
	2011/2012	Regional (GGC)	• Citalopram and escitalopram QTc prolongation reviews of patients
Economics (in addition to the above)	Ongoing	National/regional	• Practice incentive schemes for reaching agreed prescribing targets
Enforcement (although no actual enforcement in Scotland)	2002/2006	National	• Escitalopram initial rejected for use in NHS Scotland in 2002; however, accepted for use in 2006

DDD: Defined daily dose; GB£: Pound sterling; INN: International nonproprietary name; MHRA: Medicines and Healthcare Products Regulatory Agency; SSRI: Selective serotonin-reuptake inhibitor.

fell by 70.8%. There was low utilization of escitalopram throughout the study period, reaching a maximum of 6.99% of total items dispensed in 2007 before falling to 2.1% of total items dispensed in 2017 (Figure 1).

Figure 2 depicts a fall in total expenditure in recent years as more SSRIs lost their patents (Table 1).

This fall in SSRI expenditure was driven by a reduction in expenditure per item of the various SSRIs, especially after generic availability (Figure 3), with Table 3 depicting the price reductions over time for each SSRI that had lost its patent during the study period, in other words after 2001 (Table 1). Typically, the generic versions of SSRIs were dispensed once available with high rates of INN prescribing (Table 4).

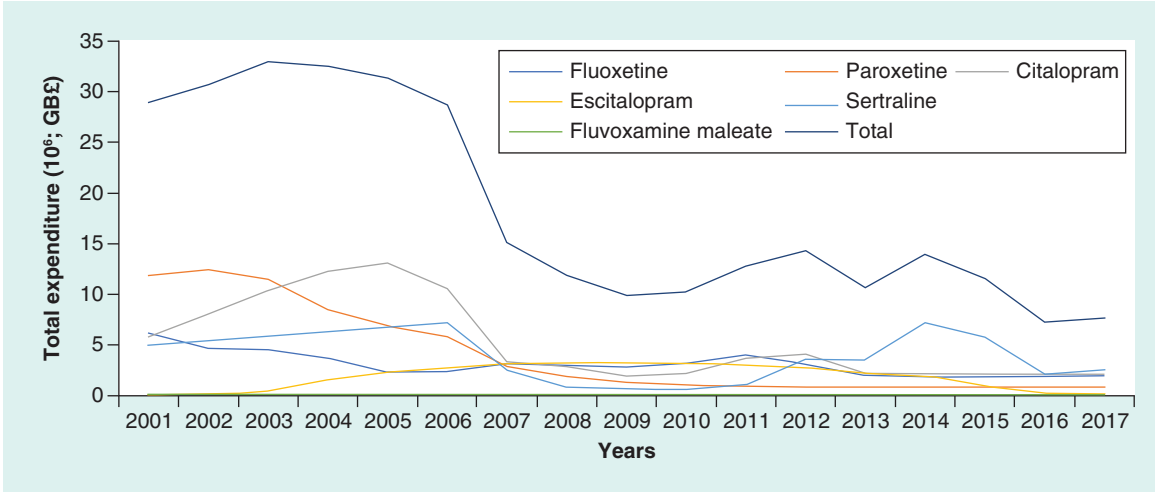

Figure 2. Total expenditure on selective serotonin-reuptake inhibitors in Scotland between 2001 and 2017.

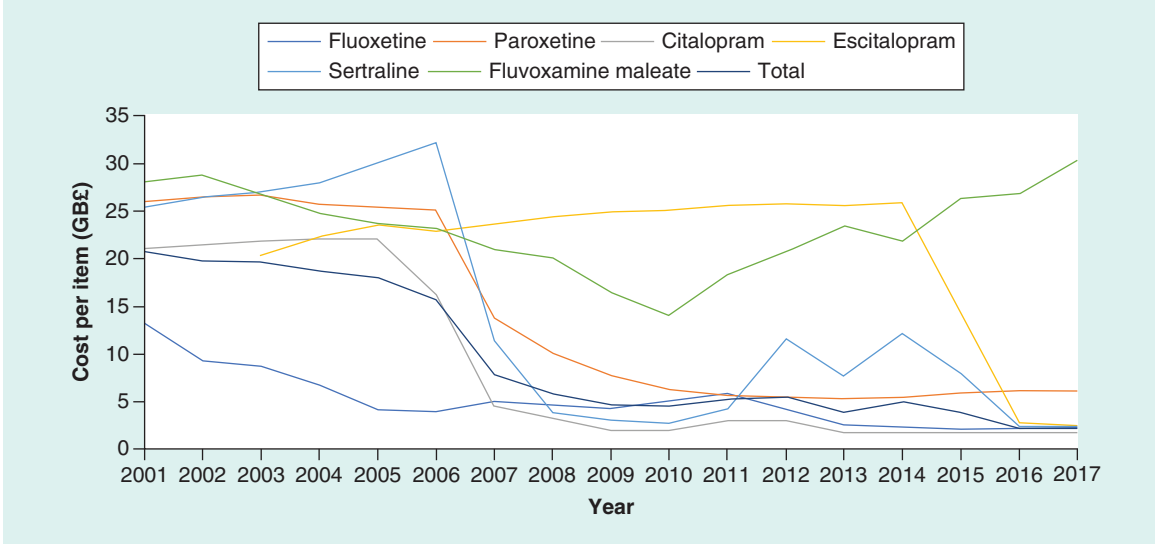

Figure 3. Cost per item dispensed for the different selective serotonin-reuptake inhibitors and total 2001–2017.

Table 3. Price reduction in expenditure/item dispensed for the various selective serotonin-reuptake inhibitors in 2017 that had lost their patent after 2001 vs their prices just before patent loss.

SSRI	% reduction in 2017
Citalopram	91.6
Sertraline	91.8
Escitalopram	90.4

SSRI: Selective serotonin-reuptake inhibitor.

Table 4. Rates of international nonproprietary name utilization (items dispensed) of regularly prescribed selective serotonin-reuptake inhibitors during the study period.

SSRI	% INN (items dispensed)
Paroxetine	91.4–98.1
Fluoxetine	98.7–99.7
Citalopram	99.5–99.9
Sertraline	98.5–99.7

INN: International nonproprietary name; SSRI: Selective serotonin-reuptake inhibitor.

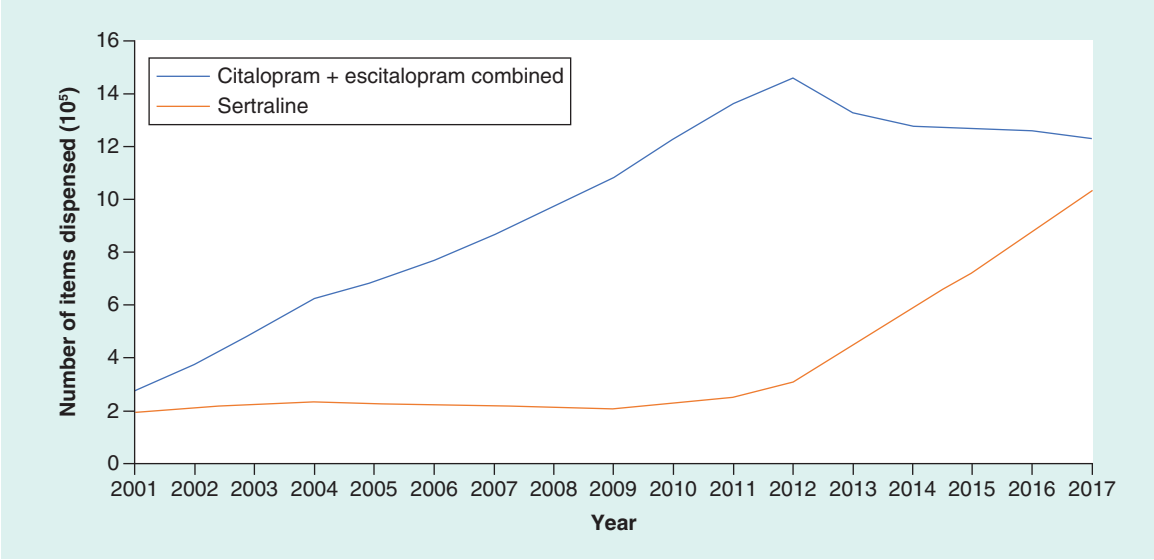

Figure 4. Extent of utilization of citalopram, escitalopram and sertraline in Scotland 2001–2017.

Differences in SSRI utilization patterns before & after concerns with QT prolongation

Figure 4 depicts the changes in the utilization (items dispensed) of citalopram, escitalopram and sertraline before and after concerns with potential QT prolongation with citalopram and escitalopram (Table 2), in other words 2001–2011 and after 2012

After the concerns with potential QT prolongation associated with citalopram and escitalopram use in 2012, there was a significant decreasing trend in citalopram and escitalopram use of 142, 951 items/year ($p < 0.001$) while the trend for prescribing of sertraline increased significantly by 141.016 items/year ($p < 0.001$).

Discussion

There has been an appreciable growth in SSRI items dispensed during the study period rising 2.34-fold (Figure 1). This may well be due to a widening of the indications for SSRIs to include anxiety as well as increasing diagnosis of depression as the diagnosis of depression and its management has not always been routinely recorded and coded as part of general practice contractual obligations [20,77], and depression has been underdetected and undertreated. This may lead to under reporting of this common illness even when patients are now more likely to seek help for their emotional distress [78]. The recent mental health and well-being survey suggests that one in six adults in England have a common mental disorder, with more people now seeking treatment [79]. The survey data from England indicates that there has been an increase in the proportion of people with clinical anxiety or depression disorders accessing mental health treatments, up from 24% in 2007 to 39% in 2014 [79]. There is no reason why Scotland should be any different from the findings in England. Patients are also receiving longer treatment [80]. Overall, we believe this growth in SSRI prescribing in Scotland in recent years (Figure 1) has been due to a combination of factors. These include SSRIs becoming available as low cost generics (Table 1; Figure 3) and adopted as first-line agents for the treatment of depression combined with additional prescribing targets (Table 2); an increase in prevalence rates and patients accessing mental health services; increasing long-term use; a lack of a regular proactive review of patients when they are stable and not in crisis; and the routine use of higher SSRI doses, which is contrary to current guidelines and evidence [17,30,43,52,77–82].

The potential associated costs with this growth in SSRI utilization have been offset by a considerable reduction in the cost/item for the various SSRIs apart from fluvoxamine (Figure 3). The price reductions seen for the various SSRIs over time (Table 3) mirror those for the lipid-lowering agents, losartan, PPIs and risperidone [15,19,83,84]. This coupled with high INN (Table 4) prescribing rates has resulted in an appreciable reduction in SSRI expenditure (73.7% reduction in 2017 vs 2001) to GB£7.613 million in 2017 (Figure 2). This is similar to the situation with lipid-lowering agents and PPIs in Scotland [15,19] providing guidance to other countries struggling with resource pressures.

The high rate of INN prescribing for the SSRIs in Scotland as a result of multiple activities (Table 2) is also similar to the situation seen with generic PPIs, statins, renin–angiotensin drugs and antipsychotics in Scotland [13,15,19,84,85]. This is encouraging and suggests no problems with the effectiveness and safety of generic SSRIs over many years. This is important for countries where there is still considerable prescribing of originator antidepressants despite the availability of good quality generics. This is not in the best interest of any key stakeholder group long term with potential resources being wasted, which could have been used to fund improved care in other situations including new medicines in patients with unmet need.

The reduction and then rise in the cost/item for fluvoxamine (Figure 3) may be a reflection of its limited use (Figure 1); consequently, limited competition and a need to reduce prices. This is seen in other situations across Europe [86]. However, this situation has made limited difference to the overall expenditure on SSRIs in Scotland with typically expenditure on fluvoxamine ranging from 0.21 to 0.85% of total SSRI expenditure during the study period.

The low utilization of escitalopram in 2007 in Scotland at 6.99% of total SSRIs dispensed (7.0% DDD basis) and 6.51% in 2008 compares favorably with 17.3% in Portugal (DDD basis) in 2007 and 30.8% in Ireland in 2008 [13] following multiple initiatives (Table 2). This is the only example of generic availability (citalopram) influencing the prescribing of patented SSRIs (escitalopram). As mentioned, general practitioners certainly in Glasgow were encouraged to switch suitable patients who were prescribed escitalopram prior to citalopram to citalopram. This was seen as an effective measure to conserve resources without compromising care with, as mentioned, typically 90% of patients remaining on citalopram at the 3-month review. Otherwise, there was no routine switching of SSRIs between patients. This was unlike the situation with the PPIs and statins in Scotland with no perceived differences in effectiveness between them [15,19]. Unlike the PPIs and statins, there were no national indicators encouraging the prescribing of particular SSRIs, although there were regional targets discouraging the prescribing of escitalopram (Table 2) [15,19,24]. This recognizes the fact that patients being treated for depression are considered more vulnerable and therefore their medication once seen as effective and tolerated is typically not changed. In addition, antidepressants certainly initially are prescribed as courses rather than life-long chronic treatment; consequently, a change to a different SSRI was generally through trying to influence the initial prescription rather than switching patients once prescribed a particular SSRI (Table 2). The situation with escitalopram was different (Table 2) as there was perceived limited clinical differences with citalopram; however, considerable differences in costs once generic citalopram became available (Figure 3).

The utilization patterns for paroxetine (Figure 1) were in line with expectations following the safety warnings; however, these were not exclusive to paroxetine although paroxetine was singled out initially [37,38,41]. In addition, concerns with the need for lengthier dose reductions following the decision to stop prescribing [43].

The significant reduction in the utilization citalopram and escitalopram, coupled with significantly increased use of sertraline in recent years, is also encouraging following safety warnings (Table 2; Figure 4). This further illustrates the favorable influence of both national and regional initiatives on effecting physician prescribing habits, which is not always the case [87–89]. As a result, again providing guidance to other countries.

Limitations

We are aware of a number of limitations with this study. This includes the fact that we were only able to analyze prescriptions dispensed and not their indication. However, two large studies in one Scottish Health Board area indicated that 87% of antidepressants were prescribed for depression, and less than 3% were prescribed for nonlicensed indications [20,77]. We could also not analyze the strength of doses prescribed to ascertain whether there were any change in the doses of SSRIs prescribed although two regional Scottish studies indicate that higher SSRIs doses are possibly being prescribed more commonly [20,78]. We are aware that there are multiple factors associated with prescribing of higher SSRI doses, including which anxiety disorders are being treated. For depression, which general practice a patient attends, if they are prescribed an SSRI for 2 years or more, and if they are coprescribed benzodiazepines and/or z-hypnotics for more than 8 weeks [20]. We also did not analyze utilization in terms of DDDs, which would have been more sensitive to changes in the doses of SSRIs prescribed; however, such studies have been undertaken. We could also not assess patient outcomes with the changes in SSRI prescribing patterns. Finally, from a safety perspective assessing the impact of the MHRA warning on the incidence of QTc prolongation and sudden cardiac death is very challenging as QT prolongation as a cause of death cannot be confirmed at autopsy. From an efficacy and wellness perspective, there are challenges with routinely collecting patient-level outcome data in ambulatory care for common mental health problems; consequently, limiting a national assessment of the impact

of SSRI prescribing. Despite these limitations, we believe our findings are robust and provide guidance for the future.

Conclusion

The considerable reduction in the cost of SSRIs over the years once generics became available has resulted in lower costs despite an appreciable increase in SSRI utilization. This is to the benefit of all key stakeholders since the savings can be used in other disease areas such as funding new medicines that address current unmet need within a resource constrained environment.

Overall, the loss of patents has not influenced SSRI prescribing patterns apart from escitalopram. This is unlike the situation seen with the PPIs and lipid-lowering medicines, and reflects the differences in the effectiveness and safety of the different SSRIs.

The changes in the prescribing patterns of paroxetine, citalopram and escitalopram are encouraging and show healthcare professionals in Scotland act quickly on safety and other warnings, providing an example to other countries.

Finally, we believe analyses such as this as part of public health psychopharmacology are justified and provide practical research findings to guide future care. Consequently, we see this discipline growing in the future.

Summary points

- There is increasing use of antidepressants including selective serotonin-reuptake inhibitors (SSRIs) in Scotland in recent years with expanding of indications, greater awareness and medicalization of depression and greater number of patients accessing treatment for their depression.
- There have also been safety concerns with some SSRIs including initially paroxetine and subsequently citalopram and escitalopram.
- The increasing availability of generic SSRIs, coupled with the need to conserve costs including limiting prescribing of patented escitalopram, and safety concerns has resulted in multiple initiatives in Scotland in recent years.
- High international nonproprietary name prescribing (up to 99.9%) and generics up to 92% below originator prices, coupled with initiatives to limit escitalopram prescribing, resulted in a 73.7% reduction in SSRI expenditure between 2001 and 2017 despite a 2.34-fold increase in utilization.
- The safety warnings resulted in a significant reduction in the prescribing of paroxetine, citalopram and escitalopram coupled with a significant increase in the prescribing of sertraline.
- Overall the multiple initiatives have increased the quality and efficiency of prescribing.

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