An investigation into the effect of advice from the Scottish Medicines Consortium on the use of medicines in Scotland's Health Service

Marion Bennie,^{1,4*} James Dear,^{2*} Sharon Hems,¹ Corri Black,³ Laura McIver⁵ & David J. Webb²

¹SMC Evaluation Team, National Medicines Utilization Unit, Information Services Division, NHS National Services Scotland, Gyle Square, Edinburgh EH12 9EB, ²Clinical Pharmacology Unit, Centre for Cardiovascular Science, University of Edinburgh, Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh EH16 1TJ, ³Section of Population Health, School of Medicine, University of Aberdeen, Forehill, Aberdeen, AB25 2ZD, ⁴Strathclyde Institute of Pharmacy and Biomedical Sciences, Strathclyde University, Glasgow G4 0NR and ⁵Scottish Medicines Consortium, NHS Quality Improvement Scotland, Glasgow, UK

WHAT IS ALREADY KNOWN ON THIS SUBJECT

Decisions on the clinical and cost effectiveness of new medicines are delivered by health technology assessment agencies such as SMC. The effect on medicine use of a decision from these agencies is unclear.

WHAT THIS STUDY ADDS

With regard to medicine use in primary care, the effect of a not recommended decision from SMC is variable. Key factors that contribute to this variability include the publication of conflicting advice by differing national bodies, failure to engage with relevant clinical experts early in the review process and a lack of alternative treatments for the indication in question. At the time of this study there were significant limitations to the data regarding medicine use within the NHS. New developments promise to improve data collection.

Correspondence

Professor Marion Bennie, Professor of Pharmacy, SMC Evaluation Team, National Medicines Utilization Unit, Information Services Division, NHS National Services Scotland, Gyle Square, Edinburgh EH12 9EB, UK.

Tel.: +44 131 275 6432

Fax: +44 131 275 7606

E-mail: m.bennie@nhs.net

*Joint first authors.

Keywords

cost-effectiveness, health technology assessment, Scottish Medicines Consortium

Received

30 June 2010

Accepted

9 September 2010

AIMS

The aims of the study were to determine the effect of advice from the Scottish Medicines Consortium (SMC) on the use of medicines within Scotland's National Health Service (NHS) and generate hypotheses that may explain differences in the impact of advice on the use of individual medicines.

METHODS

A retrospective analysis of medicine advice issued between January 2002 and December 2005 was performed. The inclusion criterion was medicines with a 'not recommended for use' decision (NRD) from the SMC (57 out of 207 medicines submitted). The exclusion criteria were medicines used predominately in secondary care and medicines with multiple indications. In total, 20 medicines fulfilled these criteria. The volume of prescribing was measured by each medicine's gross ingredient cost to the prescribing budget.

RESULTS

Before the SMC published advice there was use, though limited, of all 20 medicines. After an NRD, the pattern of use was variable, with the use of some medicines stabilizing or declining but others increasing. We identified factors to help explain unexpected use in some cases. These included delays between medicine launch and initial SMC advice, the publication of conflicting advice from different national bodies and failure to engage with relevant clinical experts early in the medicine review process.

CONCLUSIONS

This study demonstrates the complex relationship between advice following health technology assessment and change in clinical practice. When this study was done there were significant limitations in the collection of prescribing data within the NHS, which recent changes promise to improve.

Introduction

A number of countries have health technology assessment (HTA) agencies that deliver advice to their health provider on the clinical and cost effectiveness of new medicines. In Scotland, the Scottish Medicines Consortium (SMC) has the remit of providing advice to the National Health Service (NHS) about the comparative clinical and cost-effectiveness of all newly licensed medicines, all new formulations of existing medicines and all new indications for established products [1]. The SMC reviews submissions from manufacturers of medicines and aims to make decisions available within 3–4 months of product launch. The decision on a new medicine is either to accept for use without restriction; accept for restricted use or to not recommend use within the NHS in Scotland. When a 'not recommended decision' (NRD) is issued, the medicine manufacturer is welcome to resubmit to the SMC with a better case (an amended submission). It is recommended that new medicines are not prescribed prior to the SMC issuing advice and medicines with an NRD should not be prescribed in the Scottish NHS unless there are exceptional circumstances. At present there are no strict rules governing factors that define exceptional circumstances, but the patient should be significantly different from the population of patients included in the clinical trials with the condition in question and have reason to gain significantly more benefit from the drug than the average patient [1]. Therefore, for medicines with an NRD, there should be only a small volume of prescribing at most.

For a HTA organization to be effective it is essential that the advice published has a measurable impact on prescribing of medicines. Published studies suggest that the impact of advice on prescribing behaviour is variable. For example, in the USA, prescribing advice from the Food and Drug Administration (FDA) in the form of 'Dear doctor' letters can change clinical practice in some, but not all cases [2, 3]. The SMC conveys its decisions to prescribers by publishing a detailed advice document (DAD) for each medicine. The DAD is available on the SMC website and is disseminated to the area drug and therapeutics committees (ADTCs) across Scotland. The ADTCs convey the SMC decisions to their local prescribers via a range of mechanisms including electronic updates to formularies and regular prescribing bulletins. The relationship between HTA advice and medicine prescribing is complex to investigate as accurate data on the prescription of medicines are often difficult to obtain and, even if reliable data are available, there are many confounding factors that influence prescribing. In this paper we explore the relationship between prescribing of medicines and SMC advice. We investigated medicines with an NRD that had a single indication for use. Therefore, these were drugs that should have minimal, if any, use in the NHS in Scotland.

Methods

This study's inclusion criterion was medicines with an NRD reviewed by the SMC between January 2002 and December 2005. The exclusion criteria were medicines used predominately in secondary (hospital) care (excluded due to lack of available national medicine utilization data) and medicines with multiple indications (excluded because the interpretation of medicine utilization data would be limited). Data were obtained from the national primary care prescribing database, the Prescribing Information System for Scotland (PRISMS). PRISMS is a web-based application, giving access to prescribing information for all NHS prescriptions dispensed in the community for the past 5 years (<http://www.isdscotland.org/isd/5019.html>). For each medicine a 'profile' was created that included: the SMC advice, the dates of medicine launch, first SMC advice and any subsequent SMC advice, the medicine's use within the Scottish NHS before and after the publication of the SMC advice (to quantify use after advice, the period from April 2005–March 2006 was chosen because the dates of launch and SMC advice differed between medicines) and actual budget impact compared with the manufacturer's estimated budget impact (provided as part of the medicine's submission to the SMC). Medicine use was defined as gross ingredient cost (GIC) over time in pounds sterling (referred to as the net ingredient cost in England). The GIC is the cost of the medicine to the prescribing budget before any standard health board discount is applied and excludes any fees for dispensing the medicine. The number of patients treated with each medicine was estimated from the GIC, the unit cost of the medicine and the expected usual daily dose.

To identify factors that may have influenced the patterns of use of the medicines, a focus group was formed that consisted of six clinicians (senior doctors and senior pharmacists, all actively working within the NHS) from the executive committee of the SMC. The project team presented the medicine profiles to the focus group who identified common factors that may be significant in explaining the use of medicines over time, both before and after publication of the SMC advice.

Results

From a total of 207 full submissions to the SMC, 57 medicines fulfilled the inclusion criterion. Application of the exclusion criteria identified 20 medicines for study. Of these, 10 were subsequently accepted for use or for restricted use after resubmission to the SMC, six remained not recommended after resubmission and four medicines were not resubmitted for SMC review (Figure 1).

The use of medicines was investigated before and after the publication of the first SMC review (Tables 1 and 2). The median delay between medicine launch and publication

Figure 1

Medicines included in the study

Table 1

Medicine use in the time period between launch and the first SMC advice

Medicine	Time from launch of medicine to initial SMC advice (months)	Total GIC from launch to initial SMC advice (£)	Total estimated number of patients treated from launch to initial advice
Anagrelide capsules	4	7754	<10
Atomoxetine capsules	9	89 039	100–1000
Cilostazol tablets	20	104 214	100–1000
Desogestrel tablets	5	7178	100–1000
Diclofenac gel patch	4	1122	10–100
Dovobet ointment (calcipotriol/betamethasone dipropionate)	4	39 9520	>1000
Eflornithine cream	8	15 468	100–1000
Escitalopram tablets	5	209 651	>1000
Frovatriptan tablets	3	2006	100–1000
Glyceryl trinitrate rectal ointment	5	33 489	>1000
Ketotifen eye drops	19	22 640	100–1000
Macrogel 4000 powder	24	72 368	100–1000
Memantine tablets	10	97 579	100–1000
Metformin s/r tablets	2	2646	100–1000
Nicotinic acid m/r tablets	5	2684	10–100
NovoMix 30 injection (biphasic insulin aspart)	4	78 641	100–1000
Olopatadine eye drops	5	2394	100–1000
Pimecrolimus cream	2	22 254	100–1000
Solifenacin tablets	2	17 725	100–1000
Yasmin tablets (drospirenone/ethinylestradiol)	11	185 980	>1000

GIC, gross ingredient cost. The number of patients treated with each medicine was estimated from the GIC, the unit cost of the medicine and the expected usual daily dose.

of the first SMC review was 5 months (25–75% percentile 4–9.5 months). For all 20 medicines there was use, as measured by the GIC, prior to publication of the SMC advice. The estimated numbers of patients being treated was less than 1000, excepting Dovobet (betamethasone and calci-

potriol) ointment, escitalopram tablets, glyceryl trinitrate rectal ointment and Yasmin (drospirenone and ethinylestradiol) tablets.

After the SMC published their NRD following first review, 10 medicines were not subsequently accepted for

Table 2

Use of NRD medicines after the first SMC advice

Medicine	Medicine use post NRD	GIC April 2005–March 2006 (£)	Estimated treated patients April 2005–March 2006
Cilostazol tablets	Increased	135 944	100–1000
Diclofenac gel patch	Insufficient data*	NA	NA
Glycerol trinitrate rectal ointment	Insufficient data*	NA	NA
Ketotifen eye drops	Decreased	12 392	100–1000
Macrogol 4000 powder	Stabilized	67 577	100–1000
Memantine tablets	Stabilized	175 913	100–1000
Metformin s/r tablets	Increased	75 449	100–1000
Nicotinic acid m/r tablets	Increased	20 123	10–100
Pimecrolimus cream	Stabilized	65 584	>1000
Yasmin tablets	Increased	461 000	>1000

The time period studied was April 2005–March 2006. GIC, gross ingredient cost. The date of the first SMC advice was too close to the end of our study to form a conclusion regarding the pattern of medicine use for diclofenac gel patch and glycerol trinitrate rectal ointment. The number of patients treated with each medicine was estimated from the GIC, the unit cost of the medicine and the expected usual daily dose. *Launch of medicine and end of study too close to assess pattern of use. NA, not applicable as medicine received the first SMC advice after March 2006.

use either because resubmission to SMC led again to not recommended advice or no resubmission was made. The pattern of medicines' use for these 'consistently' NRD medicines was variable (Table 2), with the focus group identifying increasing use for some medicines (such as cilostazol and Yasmin, Figure 2A,B) but stabilization of use for others (such as memantine and pimecrolimus, Figure 2C,D). As memantine and pimecrolimus are treatments for chronic conditions (Alzheimer's dementia and eczema, respectively) the stabilization in GIC is likely to represent a cessation in new prescribing after the NRD.

The focus group reviewed the profile for all 20 medicines and reached consensus on factors that may explain the patterns of use. These factors are presented in Table 3.

Discussion

The SMC aims to give rapid decisions on comparative clinical and cost-effectiveness of all newly licensed medicines. This study would suggest that this is being achieved with 65% of advice issued within 6 months of medicine launch. There was use of the medicines before publication of advice. However this was relatively small (£1.4 m) in the context of a cumulative spend in the Scottish NHS primary care drugs bill, over the study period (financial year 2002/3 to 2005/6), of £3.7 billion. Among the factors identified that may explain use before the SMC advice was the delay between UK launch of medicines and initial SMC advice. This was felt to be an important factor in five of the medicines studied and supports the rapid review model used by the SMC. Although there was use before the SMC advice this should be interpreted with respect to the expenditure on other medicines in the same class. For example, before the publication of the first SMC advice the GIC for escitalopram was around £210 000. However, this is in the context

of an expenditure exceeding £16 million for all selective serotonin re-uptake inhibitors over the same time period. The marketing strategy of the pharmaceutical company may influence medicine prescription prior to the first SMC advice. Escitalopram is an enantiomer of the widely used antidepressant citalopram (manufactured by the same pharmaceutical company). At the time of first submission to the SMC, although the patent for citalopram had expired, a generic had only just been made available. This may have increased uptake of escitalopram.

For the 10 medicines that were not approved for use on resubmission or where the company did not resubmit, the pattern of use after the first SMC advice was variable. For some medicines there was a clear change in use (for example, memantine and pimecrolimus). For others, use continued to increase despite the SMC advice (for example, cilostazol and Yasmin). This inconsistent pattern of medicine use was similar to that found in England and Wales when the effect of NICE advice was studied [4]. However, the number of patients treated and the financial cost of prescription of these drugs were small in comparison with the Scottish population size (5.2 million) and cumulative expenditure in the Scottish NHS primary care drugs bill. In an attempt to identify some of the factors that may explain the variability in the impact of the SMC advice our focus groups reviewed the medicines and identified a number of potentially important issues. Firstly, a lack of effect on a medicine's use may reflect a lack of consistency in the advice prescribers receive from national bodies compared with the SMC. In the case of cilostazol, the SMC issued 'not recommended' advice but the Scottish Intercollegiate Guidelines Network (SIGN, the body responsible for clinical practice guidelines for the NHS in Scotland) recommended use in their October 2006 guideline on peripheral arterial disease [5]. This difference in guidance may have led to confusion among prescribers. Secondly, in the case

Figure 2

Medicine use for four medicines. The medicine use is measured as the gross ingredient cost. (A) cilostazol, (B) Yasmin, (C) memantine and (D) pimecrolimus

of Yasmin, the volume of prescribing (April 2005 to March 2006 GIC = £461k, compared with all standard strength combined oral contraceptives, GIC = £3.5 million) may have reflected a failure of the SMC to engage with the relevant clinical experts in the review process, leading to inconsistent professional advice.

This study highlights the limitations to the collection of prescribing data within the NHS in Scotland, particularly in secondary care. We only focussed on prescribing in primary care because, at the time of this study, there was a paucity of robust data regarding prescribing in secondary care. From 2010, there should be improved data collection in secondary care using NHS Scotland's National Hospital Medicines Utilization Database (HMUD); that will provide similar information on medicine use in hospitals to that provided by PRISMS in primary care [6]. At the time our study was performed it was not possible

to obtain patient-level data, necessary for determining which patients are being prescribed which medicine and for what duration of time. In the community, medicine prescriptions now contain the patient's Community Health Index (CHI) number, a unique patient identifier for NHS Scotland [7]. This allows us to collect patient-level data, including the actual number of patients dispensed each medicine rather than surrogate measures such as GIC. With the current system we cannot link the indication for a prescription to the medicine being prescribed. Therefore, for this study, we focussed only on medicines with a single indication. Frequently medicines will have multiple indications and advice from a HTA agency may only impact on one disease area. To obtain reliable data regarding the impact of such advice we will need the creation of a mechanism linking indication for prescribing with the specific medicine. In the future we should be

Table 3

Factors identified by the focus group that may contribute to the pattern of medicine use

Factor	Use before NRD (n = 20)	Use after NRD (n = 10)
Delay between UK launch of medicine and initial SMC advice (>9 months)	Cilostazol tablets Ketotifen eye drops Macrogol 4000 powder Memantine tablets Yasmin tablets	NA
Limited use relative to alternative treatments	Escitalopram tablets Yasmin tablets Atomoxetine capsules	Macrogol 4000 powder Metformin s/r tablets Nicotinic acid m/r tablets
No alternative licensed products	Glycerol trinitrate rectal ointment	Glycerol trinitrate rectal ointment Memantine tablets
Influence of pharmaceutical industry marketing strategy	Escitalopram tablets NovoMix 30 injection Dovobet ointment	
Variation in advice issued by national bodies to NHS boards and clinicians	NA	Cilostazol tablets Pimecrolimus cream
Lack of engagement of relevant clinical experts in early stages of SMC	NA	Yasmin tablets

NA, not applicable

able to repeat our study and obtain more robust patient-level data to address what impact an HTA agency's advice has on prescribing. We believe our study is worth repeating as, in the time period since we performed this study, the impact of SMC advice on the use of medicines may have increased significantly as a result of a number of Scottish Government publications that clarify and strengthen the remit of the SMC [8–10].

This study demonstrates the complex relationship between advice following health technology assessment and change in clinical practice. Factors that may explain the patterns of medicine use include delays between medicine launch and initial SMC advice, the publication of conflicting advice from different national bodies and failure to engage with relevant clinical experts early in the medicine review process. At the time of this study there were significant limitations in the collection of prescribing data within the NHS. Recent changes promise to improve significantly the quality of data available regarding the prescribing of medicines.

Competing Interests

There were no competing interests.

We would like to thank members of the SMC Evaluation Team, which included W.D. Ramsay, S.D. Oduro, V. Cairns and J. Nicholson.

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