

Nurse supplementary prescribing for patients with diabetes: a national questionnaire survey

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Aims and objectives. To examine the prescribing practices of nurse supplementary prescribing in diabetes.

Background. Nurses in several roles are involved in the management of medicines for patients with diabetes. Nurse prescribing should help optimise these roles. Nurses in the UK have virtually the same independent prescribing rights as doctors. There is little or no evidence on the extent to which nurse supplementary prescribing is used, or the impact and activity of nurse supplementary prescribing for patients with diabetes.

Design. Survey.

Method. A random sample of 214 nurse supplementary prescribers self-completed a written questionnaire.

Results. The majority of nurses held an academic qualification at degree level or higher, had a wealth of clinical experience, worked full-time, were based in primary care and worked in general practice. The majority of nurses prescribed between one and five items a week. Oral anti-diabetic drugs, hypertension and lipid-regulating drugs and insulins were the products most often prescribed. Over 85% had undertaken specialist training in diabetes prior to undertaking the prescribing programme.

Conclusion. Supplementary prescribing provides a practical and useful framework within which to prescribe medicines for patients with diabetes and its associated complications. Specialist diabetes training is a necessary prerequisite for nurses prescribing in this area. It is evident that there is still a place for supplementary prescribing.

Implications for clinical practice.

- Recent legislative changes mean that nurses can now independently prescribe practically any drug.
- Nurses in general practice appear to prescribe most frequently as a nurse supplementary prescriber for patients with diabetes.
- Nurse supplementary prescribers are likely to use this mode of prescribing to deliver medicines to patients with diabetes.

- Over two-thirds prescribe for common but serious complications of diabetes, e.g. hypertension, hyperlipidaemia and cardiovascular disease

Key words: diabetes, nurse supplementary prescribing, nurses, nursing, UK

Introduction

Diabetes mellitus (DM) is one of the most common chronic diseases in both western and developing countries. Approximately 194 million people (5%) of the worldwide population currently suffer from this condition (Audit Commission 2000). The care of people with diabetes is complex. A quarter of people living with this disease also experience three or more other long-term conditions (Audit Commission 2000). In addition to the personal effects of such co-morbidities, much of the five million pounds a day spent in the UK by the National Health Service (NHS) on its treatment (DoH 2003a), could be reduced with good healthcare and good self-management (DoH 2003b).

The emphasis placed on the role expansion of nurses (DoH 1999), the need for staff to work together to reduce waiting times and deliver modern patient-centred services (DoH 2000) has meant that nurses-led care is seen as one means of improving health care provision. There is evidence that nurses have lead roles to play in the delivery of care in a number of areas, especially chronic diseases (Campbell 2004, McKee & Nolte 2004, Raftery *et al.* 2005, Courtenay & Carey 2006). It is evident that nurses working in several roles are involved in the treatment management of patients with diabetes (Carey & Courtenay 2007). These roles have developed in recognition of the fact that access to health professionals, who are skilled in insulin therapy and the management of diabetes, is vital to reduce long term complications and improve bed states (National Institute of Health 2005). The role of the nurse in service delivery for diabetes patients is emphasised by the *National Service Framework for Diabetes* (NSF) (DoH 2003a) and the prescription of medicines by nurses should help optimise this role.

In the UK, appropriately qualified community nurses are able to assess, diagnose and prescribe independently from a limited list of medicines included in the *Nurse Prescribers' Formulary for Community Practitioners* (NPF). Nurse independent prescribers (NIP) (previously known as independent extended prescribers) are similarly able to assess, diagnose and prescribe any licensed medicine [and some controlled drugs (CDs)] independently (DoH 2006). By contrast, nurse supplementary prescribing (NSP) (DoH 2003b) takes place

after an assessment and diagnosis of a patients condition has been made by a doctor and a Clinical Management Plan (CMP) has been drawn up for the patient. The CMP includes a list of medicines from which the supplementary prescriber is able to prescribe (DoH 2003b). Supplementary prescribers are able to prescribe any medicine (including unlicensed medicines and CDs), but, it is best suited to the management of chronic and long-term conditions such as DM.

Training for NIP and NSP is combined, i.e. nurses successfully completing the prescribing programme are awarded the dual qualification of nurse independent/supplementary prescriber (NISP). Additionally, nurses need to acquire specialist knowledge prior to undertake the prescribing programme [Nursing and Midwifery Council (NMC) 2006]. This knowledge may be attained in a number of ways, e.g. university accredited modules or through experiential learning. There are now over 10 000 nurses across the UK able to prescribe both as NISPs (NMC 2007).

Given the recent legislative changes surrounding the prescription of medicines by nurses it is important to evaluate the success or otherwise of these developments and also to identify key issues that are likely to arise. There is very little or no evidence of NSP and how this mode of prescribing is used to manage patients with diabetes.

Background

Three studies (Craddock & Avery 1998, Winocour *et al.* 2002, Courtenay *et al.* 2006) provide evidence that nurses, caring for patients with diabetes, are involved in medicines management. Winocour *et al.* (2002) surveyed 456 consultant physicians providing diabetes services across 238 acute NHS trusts and units. It is unclear how many physicians returned the completed 92 item questionnaires; however, consultants providing services to over 75% of the trusts responded. Information collected from 75% of the sample, indicated that diabetes specialist nurses (DSNs) were involved in adjusting medicines for hypoglycaemia. Additionally, respondents reported that over 90% of these nurses had received training to educate patients and staff about diabetes.

Specifically looking at the role DSNs play with regards to the practice of prescribing and adjusting insulin dose,

Craddock and Avery (1998) distributed surveys in 1993 and 1996 to 50 DSNs, in the South West Thames Region. Of the 71 questionnaires distributed across the two surveys, over 70% of the nurses responded. Nurses completing the questionnaires in 1996 reported that they were less likely to consult doctors when changing the dose of insulin or changing the insulin regime. However, they were more likely to have agreed with the doctor the extent to which insulin dose could be altered. Additionally, participants in 1996 were more likely to adjust insulin dose over the telephone, dispense insulin from an agreed stock, use presigned prescriptions or supply patients with prescriptions with medical countersignatures. In contrast to findings reported by Winocour *et al.* (2002), only 20% of these respondents reported that they had undergone any formal training in diabetes.

Although not specifically focusing on diabetes, Courtenay *et al.* (2006) undertook a survey to provide a national perspective of independent extended/supplementary nurse prescribing practice. Respondents in this survey ($n = 868$) were asked to identify the conditions for which they prescribed most frequently using supplementary prescribing. Diabetes was one of the most common conditions cited.

As well as managing medicines for diabetes, there is evidence to suggest that nurses are effectively managing some of the common complications including hypertension, hyperlipidaemia and cardiovascular disease (Denver *et al.* 2003, New *et al.* 2003). New *et al.* (2003) used a randomised controlled trial (RCT) (involving over 1500 patients) to examine the effect of specialist nurses on raised blood pressure, raised total cholesterol and mortality. It was evident from the findings that a higher number of patients seen by the specialist nurse achieved their treatment targets and there was a significant reduction in patient mortality. Further support for these findings are provided by Denver *et al.* (2003). Data collected from the 120 patients involved in this RCT identified that patients who attended the nurse-led clinic were three times more likely to reach a target systolic BP < 140 mmHg. Additionally these patients experienced a significant reduction in 10 years coronary heart disease and stroke risk scores.

Although not specifically focusing on diabetes, size and make up of the practice population (Luker *et al.* 1997, 1998) and nurses' role (Luker & McHugh 2002, While & Biggs 2004, Hall *et al.* 2006) have been reported by researchers as factors influencing the low prescribing rates reported by District Nurses (DN) and Health Visitor (HV) prescribers.

Three studies (Larsen 2004, Latter *et al.* 2005, Courtenay *et al.* 2006) have examined the prescribing patterns of independent extended nurse prescribers. In line with the low prescribing rates of DN/HV prescribers, Larsen (2004) in a

survey of 307 nurse managers (working in accident and emergency departments, minor injury units and walk-in-centres) reports that only 27 of 55 nurses who had undergone independent extended prescribing training were prescribing medicines.

These findings are in contrast to those reported by Latter *et al.* (2005) and Courtenay *et al.* (2006). Over 90% of the 246 independent extended nurse prescribers surveyed by Latter *et al.* (2005) and nearly 90% of the 868 independent extended/supplementary prescribers surveyed by Courtenay *et al.* (2006) used independent prescribing. Interestingly, only 35% of the respondents in Courtenay *et al.*'s (2006) study reported that they had used supplementary prescribing.

Restriction of local arrangements has recently been identified as a further factor that influences the prescription of medicines by nurses. Findings by Hall *et al.* (2006), involving the collection of semi structured interview data (from 23 HV and DN prescribers and five prescribing leads) and questionnaire data (from 44 DNs and HVs) across three Strategic Health Authorities, identified that some nurses had to wait several months to receive their prescription pad and so were unable to prescribe once qualified. Nurses sampled by these researchers also identified a lack of access to the patient's medical records as a further barrier to prescribing. Additionally, the paperwork involved in writing a prescription, arranging delivery and issuing repeat supplies of an item, were identified by respondents as reasons to send the patient to the general practitioner for a prescription. Restrictions at a local level, including lack of prescribing pads, absence of prescribing budgets and inability to computer generate prescription were also identified by Courtenay *et al.* (2006) and Latter *et al.* (2005) as factors which prevented the prescription of medicines by independent extended/supplementary prescribers.

The evidence emerging from the literature indicates that medicines management is an area of care in which nurses, caring for patients with diabetes, are involved. These nurses are also managing the medicines for some of the common complications of this disease. Evidence examining the rate at which nurses prescribe medicines is conflicting and a number of factors have been reported as influencing the prescription of medicines by nurses. There is no evidence currently available specifically examining NSP for patients with diabetes. This is important given that diabetes has been identified as a condition for which NSPs prescribe most frequently.

Aim

The aim of the study was to provide a national evaluation of NIP and NSP in diabetes in the UK. A key component

was to examine the prescribing practices of nurses who use supplementary prescribing to prescribe medicines for patients with diabetes. This component forms the focus of this paper.

Methodology

A survey design was used with a postal questionnaire. The data were collected between October and December 2006.

Sample

The participants were 214 nurses located throughout the UK. All nurses were qualified NISPs and registered on the NMC data base. All prescribed medicines for patients with diabetes.

One thousand nine hundred and ninety two nurses were selected at random from all ($n = 8000$) nurses registered on the NMC database of NISPs, i.e. 25% of all NIPs/NSPs across the UK. Based on the findings and response rate of previous national surveys undertaken by researchers (Latter *et al.* 2005, Courtenay *et al.* 2007), it was estimated that a 70% response rate would be achieved of whom 30% of respondents would prescribed medicines for patients with diabetes. This large sample was required to ensure that each one of the broad range of settings in which nurses prescribe medicines for people with diabetes is represented. After one follow up reminder questionnaire, 1400 (70%) questionnaires were returned, of which 1377 were completed. Twenty three were not completed as participants were no longer working in practice or were working abroad. Of the 1377 completed questionnaires, 439 participants prescribed for diabetic patients and 214 used NSP. This paper reports on the findings for these 214 nurses.

Questionnaire

Simple instructions with regards to how to complete the questions were provided on the first page of the booklet. The first section of the questionnaire collected some general demographic information. This included job title, participants Grade/Band (i.e. level of clinical expertise and band/grade in which the individual is placed and paid, band 5/E = low, band 9/I = high), whether they worked full time or part time, if they worked in primary and/or secondary care, their age, highest academic qualification and prior to undertaking the prescribing programme, what if any specialist training they had undertaken. The sample was then asked to identify the length of time they had been qualified as a NISP and how much experience they had acquired in their main area of practice before undertaking the prescribing

programme. They were also asked to identify the methods they had used to deliver medicines to patients since they had qualified as a prescriber.

Participants were then asked to list problems they had encountered that had hampered or prevented NSP in diabetes. Respondents were next asked to indicate what percentage of time each week they devoted to diabetes and the number of items they prescribed as NSP in a typical week for patients with diabetes (i.e. 0, 1–5, 6–10, 11–20, 21–30, 31–40, 41–50, 51+) and which conditions/products they prescribed for these patients. Tick boxes were supplied to indicate responses.

Reliability and validity

A questionnaire booklet was developed for the purpose of the study. Its content was developed from previous work involving independent extended and supplementary nurse prescribers (Latter *et al.* 2005, Courtenay *et al.* 2006), a search of the literature of nurse-led care in diabetes (Carey & Courtenay 2007) and the *Nurse Prescribers Formulary (2005–2007)* (BMA 2005). To pilot the questionnaire 20 qualified NISPs who prescribed for diabetic patients were asked to complete it. After doing so, they were asked to comment on its ease of completion and if they experienced any difficulties understanding what was required of them at any point throughout the questionnaire. It was evident from the completed questionnaires that both the format and content of the questions were appropriate. Only minor refinements and amendments were made. Following data entry of the completed questionnaires 10% were then reviewed by one of the authors (NC).

Data collection

Participants were sent a letter outlining the purpose of the study (and what would be required of them), an information sheet and a copy of the questionnaire. The information sheet outlined the study aims and what participants would be required to do. It also informed participants that the study was completely voluntary (and emphasised that individuals could withdraw at any point if they wished to do so), that responses were strictly confidential, that information collected from the questionnaire would be made anonymous and that no identifying information would emanate from the research.

Ethical approval

A full research proposal was submitted for scrutiny by the Berkshire Research Ethics Committee and the University of

Reading Ethics Committee. The study met the research governance criteria of these committees. Approval to undertake the study was therefore granted. Questionnaires were sent to the home address of participants. Return of a completed questionnaire was taken as consent to participate.

Data analysis

Microsoft Excel and SPSS version 14 were used for data entry and analysis. Chi Square tests were used to investigate how the number of items prescribed varied according to job title, age, specialist training in diabetes. Themes in qualitative data were identified, coded and analysed using content analysis.

Results

Demographic details

The demographic data of the sample including job title, grade/band, part/full time work, area of work, age, academic qualification, time since qualified as NIP/NSP and years of experience in area of practice before undertaking the prescribing course are presented in Table 1.

Specialist training

One hundred and thirty-seven (64.0%) indicated that they had undertaken a diploma, degree and/ or masters level module prior to undertaking the prescribing programme. Ninety-six (44.9%) had attended university accredited study days. Forty-six (21.6%) had undergone informal training. This included visits to a specialist nurse or doctor working in a diabetes department, in-house training and training provided by drug companies. Twenty-nine (13.6%) had not undertaken any specialist training in diabetes.

Problems hampering or preventing nurse supplementary prescribing in diabetes

Participants were asked to describe the problems they had encountered which were specific to diabetes prescribing. These problems were analysed using content analysis.

Table 2 presents the categories that arose from this analysis. Sixty six responses were given. Fifty-nine per cent ($n = 39$) of NSPs who reported problems indicated that these were of a practical nature including access to and lack of a prescribing pad, inability to computer generate prescriptions, access to notes and communication.

What proportion of your time each week is spent on diabetes?

Participants were asked to indicate what percentage of time each week they devoted to diabetes. One hundred and fifteen (54%) indicated that this was less than 20%. Fifty-six (26%) reported this to be between 20–50%. Thirty (14%) participants reported that more than 50% of their week was devoted to diabetes.

In a typical week how many items do you supplementary prescribe for patients with diabetes?

The number of items prescribed in a typical week as an NSP is presented in Table 3. Nearly thirty per cent ($n = 46$) of respondents prescribed between one and five items a week, however, over 40% ($n = 63$) prescribed more than six items a week. Over 50% ($n = 50$) of general practice nurses prescribed more than six items in a typical week. Thirty-three per cent of specialist nurses ($n = 10$), 14% of senior nurses ($n = 1$) and only 9% ($n = 2$) of community nurses prescribed six or more items in a week. The differences between groups were statistically significant ($p = 0.001$). However, neither age, nor the benefit of specialist training in diabetes, or confidence in diabetes prescribing had a significant effect on the number of items prescribed ($p = 0.871, 0.279, 0.218$, respectively).

Conditions/products prescribed by NSPs

Table 4 describes the conditions/products that NSPs prescribe for diabetic patients. About 75% ($n = 106$) of NSPs prescribe oral anti-diabetic drugs, while 66.0% ($n = 93$) prescribe for hypertension and lipid regulating drugs, 64% ($n = 90$) for cardiovascular disease and 56% ($n = 79$) insulin.

Participants were asked to list the three things prescribed most often as a NSP for patients with diabetes. The most often listed were oral anti-diabetic drugs (66.9%), hypertension (47.9%), lipid regulating drugs (29.0%) and insulin's (36.4%). General Practice nurses prescribed a significantly broader range of about five products, followed by specialist nurses (four products/conditions) ($p = 0.031$) (see Table 5).

Discussion

Before summarising the key findings and drawing conclusions, a potential limitation of our study must be taken into account. Respondents were asked to report on the products they had prescribed along with the factors that had hampered or prevented prescribing in diabetes. It

Table 1 Demographic characteristics

Job title	n	% of total sample
General practice (practice nurses and nurse practitioners)	141	66.4
Specialist nurses (clinical nurse specialists, specialist nurse practitioners, nurse clinicians, children's nurses and midwives)	33	15.4
Community nurses (community/modern matron, HV, DN, community children's nurse specialist, community psychiatric nurses and learning disabilities)	26	12.1
Senior nurses (nurse consultants, senior nurses, charge nurses, sisters, manager)	12	5.6
Grade/Band		
Grade F/G or Band 6	51	23.8
Grade H or Band 7	101	44.4
Grade I or Band 8/9 or nurse partner	46	21.5
Part time/full time		
< 20 hours/week	18	8.4
21–30 hours/week	76	35.5
Full time, i.e. > 30 hours/week	118	55
Primary/and or secondary care		
Primary care	177	82.7
Secondary care	21	9.8
Primary and secondary care	15	7.0
Age		
< 35 years	15	7.0
36–45 years	83	38.8
46–55 years	89	41.6
55–65 years	26	12.1
Academic qualification		
Certificate level	4	1.9
Diploma level	31	14.5
Degree level	128	59.8
Master level	48	22.4
PhD	3	1.4
Time since qualified as NIP/NSP		
< 6 months	3	1.4
6–12 months	20	9.3
1–2 years	73	34.1
> 2 years	114	53.3
Experience in area of practice before NIP/NSP		
< 1 year	3	1.4
1–2 years	8	3.7
2–5 years	26	12.1
> 5 years	175	5

Percentages do not add to 100% in each category as some participants did not complete every question.

would have been helpful to have also asked respondents to indicate which products they had prescribed and the factors that had hampered or prevented prescribing in diabetes in the last six months. The majority of respondents had been qualified in excess of two years. Factors that had originally hampered or prevented prescribing may now not exist. Additionally, methods used within the last six months may have differed from those used upon initial qualification. This additional data would have provided a fuller picture of current practice.

The majority of nurses in our sample held an academic qualification at degree level or higher, had a wealth of clinical experience, work full-time, were based in primary care and worked in general practice. Nearly half the participants who prescribed for diabetes (48.7%) reported that they had prescribed using NSP.

These findings are consistent with those reported by Courtenay *et al.* (2006) and Latter *et al.* (2005). More than 80% of the nurses sampled in these two previous studies reported they used independent extended prescribing and that

Table 2 Problems faced by nurse supplementary prescribers with respect to prescribing in diabetes

	<i>n</i>	%
Practical problems, e.g. lack of resources	39	59.1
Lack of clinical knowledge, competence, patient compliance	18	27.3
Employer restriction/objections by pharmacist, etc	16	24.2
Total number of responses	66	

Percentages do not add to 100% since respondents have generally more than one problem.

Table 3 Number of items prescribed using nurse supplementary prescribing in a typical week to diabetic patients

Number of items	Frequency	%
0	47	30.1
1–5	46	29.5
6–10	31	19.9
11–20	23	14.7
> 20	9	5.8
Total	156	100.0

Table 4 Conditions/products being prescribed using nurse supplementary prescribing for people with diabetes

Conditions/products	NSP (<i>n</i> = 141)	
	Frequency	%
Oral anti-diabetic drugs	106	75.2
Hypertension	93	66.0
Lipid regulating drugs	93	66.0
Cardiovascular disease	90	63.8
Insulin's	79	56.0
Management of micro-albuminuria	64	45.4
Insulin pens, syringes and needles	62	44.0
Obesity	61	43.3
Monitoring (glucose, etc.)	59	41.8
Hypoglycaemia	55	39.0
Diabetic neuropathy (including erectile dysfunction)	43	30.5
Fungal skin infection	39	27.7
Smoking cessation	39	27.7
Varicose eczema – atopic/contact dermatitis	38	27.0
Immunisation – flu/pneumonia	37	26.2
Leg or foot ulcers (chronic skin)	29	20.6
Diabetic ketoacidosis	26	18.4

Percentages do not add to 100% since respondents have generally prescribed more than one product.

their highest academic qualification was at degree level of above. Compared with previous findings, more nurses in our sample (over 65% compared to 39% reported by Latter *et al.* and 54% by Courtenay *et al.*) worked in general practice.

Nearly 50% of the participants in our study reported that they used supplementary prescribing and 70% of these

Table 5 Mean number of conditions/products prescribed as a nurse supplementary prescriber according to job title

Job title categories	Mean	SE	95% CI	
			Lower bound	Upper bound
General practice	5.2	0.413	4.393	6.021
Specialist nurses	3.9	0.864	2.172	5.578
Community nurse	2.8	0.958	0.957	4.736
Senior nurses/managers	2.0	1.545	–1.047	5.047

respondents reported that they prescribed between one and six items a week. This is higher than that reported by Courtenay *et al.* (2006) who identified that just over a third of their sample used supplementary prescribing, the majority of respondents reporting that they prescribed less than five items a week for skin conditions. Respondents in our study also prescribed a greater number of items than DN/HV prescribers, these nurses frequently prescribing less than one item per week (Hall *et al.* 2006).

In addition to prescribing drugs for diabetes, our findings show that over two thirds of respondents also prescribed for common complications of diabetes including hypertension, hyperlipidaemia and cardiovascular disease. These findings are in line with those reported by previous research (Denver *et al.* 2003, New *et al.* 2003). Hypertension, hyperlipidaemia and cardiovascular disease are also areas in which nurses in these studies prescribed medicines. Our findings are also consistent with policy literature (DoH 2006, NMC 2006) where supplementary prescribing is described an ideal mechanism for the treatment of chronic long-term conditions.

The fact that NSP was used to prescribe a broader range of products by nurses in general practice (the majority of whom also devoted less than 20% of their week to diabetes), perhaps provides some evidence that supplementary prescribing is a useful mechanism to treat patients with multiple pathologies, where a team approach to care is necessary. Such nurses may only feel confident to prescribe for these conditions when using a CMP (NMC 2006).

Over 85% of participants in our study reported that they had undertaken specialist training in diabetes (i.e. a diploma, degree, or masters level module in diabetes or accredited study days) prior to undertaking the prescribing programme. This finding is consistent with those reported by Winocour *et al.* (2002) who reported that nearly all DSNs in their research had received training to educate patients and staff about diabetes. It is interesting to note that the NMC prescribing guidelines (NMC 2006). The NMC guidelines stipulate that nurses need to acquire specialist knowledge prior to undertaking the prescribing programme (NMC

2006), however, 14% of our sample had not undertaken any specialist training in diabetes.

Participants in our sample reported several factors hampering or preventing supplementary prescribing in diabetes. Practical problems (including access to and lack of prescribing pad, inability to computer generate prescriptions, access to notes and communication) were the most frequently cited by 18% ($n = 39$) of nurses. Lack of clinical knowledge and competence were cited by 8.4% ($n = 18$) of the sample. This is in line with Courtenay *et al.* (2006) who reported that nearly 20% of the nurses in their study had experienced similar practical problems implementing prescribing.

Although the software to computer generate prescriptions is now available and restriction of local arrangements may have been resolved shortly after the nurses in our sample had qualified, such restrictions have been identified as a barrier to prescribing by other researchers (Latter *et al.* 2005, Courtenay *et al.* 2006, Hall *et al.* 2006). These are areas that warrant further exploration. The fact that nurses reported that clinical knowledge had prevented them prescribing, confirms that these nurses are aware they must only prescribe within their scope of practice and competence (NMC 2006). This is reassuring bearing in mind that nurses now have practically the same prescribing rights as doctors.

Despite the evidence that there have been implementation problems surrounding supplementary prescribing and nurses are now able to independently prescribe practically any licensed medicine, our findings indicate NSPs are likely to use this mode of prescribing to deliver medicines to patients with diabetes.

Conclusion

Our findings suggest that modern patient-centred services are supported by the effective use of supplementary prescribing by nurses who prescribe for patients with diabetes. As nurses working in a variety of roles are involved in the care of patients with diabetes, our findings may be of interest to policy makers, practitioners and educationalists involved in this area of practice. It is evident that there is still a place for supplementary prescribing.

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Contributions

Background: NC/MC; Methodology: NC/MC; Results: NC and Discussion: NC/MC

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