Interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review

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Title: Interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review

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ABSTRACT

Objective: To summarise evidence on the effectiveness of interventions to encourage prescribing of generic forms of prescription drugs where clinically appropriate in the UK NHS and similar settings.

Design: systematic review

Search strategy: We conducted a rapid evidence synthesis in two stages: Firstly, we searched databases such as the Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE), for systematic reviews of interventions that reported outcomes related to utilisation of generic drugs. For the second stage, we searched several databases including MEDLINE and EMBASE to identify primary studies of any interventions not adequately covered by systematic reviews.

Data extraction and quality assessment: Data were extracted into a standardised data extraction form. Standardised quality assessment tools were used to assess study quality. Two reviewers were involved in data extraction and quality assessment.

Results: Ten reviews were included for the initial evidence synthesis but most were of limited usefulness to our focused review question. One review evaluated the effect of prescribing policies using financial incentives and showed an increase in generic prescribing. Thirteen primary studies of other interventions were included for the rapid review. Two studies showed an increase in percentage of overall generic prescribing with an educational intervention; two studies showed improvement in generic prescribing rates when physicians collaborated with pharmacists, though in one study this was not statistically significant; two US studies showed improvements in generic prescribing with electronic prescribing. Five out of seven studies showed positive results with multi-faceted interventions.

Conclusions: The existing evidence remains insufficient to determine which intervention or combination of interventions is most effective due to methodological weaknesses and conflicting results. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

Article Summary

'Strengths and limitations of this study'

- Appropriate use of generic medicines is important for healthcare systems to make optimum use of limited resources. In England, rates of prescribing by generic name are over 80% overall but there is evidence of variation between regions and individual prescribers.
- We have synthesised evidence from systematic and primary studies that have evaluated the effectiveness of interventions to promote generic prescribing at the level of the individual prescriber or GP practice.
- The study brings together evidence on a wide range of interventions and identifies a number of potentially effective approaches.
- Limitations of the evidence base make it difficult to draw any firm conclusions about the relative effectiveness of different approaches. Recent evidence from UK NHS settings is particularly lacking.
- Given the uncertainty around the evidence base, decision-makers in settings where only small improvements in generic prescribing rates are likely to be achievable should take into account the practicality and costs of the intervention before implementing measures designed to further increase generic prescribing rates.

BACKGROUND

Generic medicines, which are the substitutes of original (branded) medicines with the same quality, safety and efficacy, [1] offer an interesting opportunity for governments and healthcare payers to contain escalating healthcare budgets as their prices tend to be 10–80% lower than their proprietary equivalents.[2] In England the proportion of prescriptions prescribed generically (i.e. by non-proprietary name rather than brand name) increased from 76% in 2002 to 83.6% in 2012.[3]

Despite the trend of increasing generic prescribing rates there is thought to be room for greater efficiency. In 2008 approximately 5% of medicines were prescribed by their brand name in England when there was a generic alternative available.[4] A national Audit Office report in 2007 reported that prescriptions of generic statins (simvastatin and pravastatin) varied from 28% to 86% across English Primary Care Trusts.[5] More recent research has also identified marked variation in generic prescribing by GPs (for data on statin prescriptions in England, see www.prescribinganalytics.com).

In 2009, the Department of Health consulted on a proposal for the introduction of generic substitution (allowing pharmacists to fulfil a prescription for a branded medicine by dispensing a generic equivalent) in primary care in England. However, after considering the responses to the consultation, the Government decided not to progress the proposal further.[4] As an alternative it was suggested that 'other, less nationally prescriptive mechanisms for further supporting the use of generic medicines can be explored'.

We have undertook a rapid evidence synthesis to inform decision-makers about the evidence base for interventions that might be applied to increase generic prescribing at the level of the individual or small units such as general practices.

Aims/objectives

To identify and summarise relevant research evidence using existing synthesised evidence sources (systematic reviews) supplemented as necessary by a rapid systematic review of primary research. The project aims to benefit the UK NHS by increasing the accessibility of the relevant evidence and by identifying gaps that need to be filled by further research.

Methods

We conducted this rapid evidence synthesis in two stages: an initial mapping of existing sources of synthesised evidence followed by rapid systematic review of the primary research literature, for interventions not covered by previous reviews. We registered the protocol of this review on PROSPERO the international prospective register of systematic reviews (registration number CRD42013004443).

Mapping of synthesised evidence

We searched the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment (HTA) database and Health Systems Evidence for the systematic reviews to map the existing sources of synthesised evidence. Terms relating to prescribing were combined using the Boolean operator AND with terms for generic drugs. No date or language limits were applied.

Systematic reviews, HTA reports and overviews were included if they evaluated the effectiveness or efficacy of an intervention and reported an outcome or outcomes related to utilisation (prescribing or dispensing) of generic drugs regardless of indication, setting or type of healthcare system. One reviewer examined the search results to identify potentially relevant reports. Full texts of potentially relevant reports were assessed for inclusion by two reviewers independently. Any disagreements were resolved by discussion and if necessary by involving a third reviewer.

Essential details of included reports were extracted using a simple data extraction form. These included the stated objectives, inclusion criteria, period covered by the search, interventions in included studies, main results and authors' conclusions. Data were extracted by one reviewer and checked by a second. The results were synthesised narratively and used to guide searching of the primary literature. In particular, interventions considered to be adequately covered by existing synthesised evidence were excluded from the rapid review of primary literature.

Rapid review of primary literature

Selection of studies

For the second stage, the previous search strategy described above was adapted for use in databases containing primary studies. We searched PubMed, MEDLINE, MEDLINE In-Process, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index of Nursing and Allied Health (CINAHL), EMBASE, Health Management Information Consortium (HMIC) and PsycINFO for studies published in English language during the period between 1985 and 2013 (see supplementary).

Primary studies evaluating interventions designed to promote prescribing and/or dispensing of generic drugs were included. Studies which looked at the financial incentives as a main intervention were excluded as there were already reviews covering those aspects in generic prescribing. We excluded interventions considered not applicable in UK NHS settings and also generic substitution because the Department of Health decided after a consultation exercise not to introduce such a policy. Randomised or quasi-randomised controlled trials, controlled before-and-after (CBA) studies and interrupted time-series (ITS) were eligible. The primary outcome was any measure of rate of prescribing or dispensing of generic drugs (relative to comparator group or change over time). Studies of barriers and facilitators of generic prescribing were also included but this will be reported elsewhere (a full report is available from the authors).

Records were initially screened by one reviewer to remove obviously irrelevant material, the remaining records and full papers were screened independently by two reviewers. Any disagreements were discussed with a third reviewer.

Data extraction and quality assessment

Data on objectives, setting, study design, participants, details of the intervention(s) and results/conclusions related to rates of generic prescribing/dispensing were extracted. Risk of bias was assessed using the criteria of the Cochrane EPOC (Effective Practice and Organisation of Care) Group. This was undertaken by one reviewer and checked by a second; disagreements were resolved by discussion.

Methods of synthesis

The substantial heterogeneity of interventions and method across studies precluded meta-analysis and we therefore reported in a narrative synthesis. Studies were grouped by type of intervention or interventions.

Results

Mapping of synthesised evidence

The search identified 356 potentially relevant references: 40 full papers were ordered; 10 systematic reviews (9 reviews and one overview of reviews) which evaluated interventions such as financial incentives, prescribing policies, cost sharing, use of computers/IT, educational interventions, audit and feedback (Table 1).

Most of the reviews had broad objectives and did not focus specifically on interventions targeted at increasing rates of generic prescribing, for example they looked at prescribing behaviour in general rather than specifically generic prescribing. As a result there was often limited synthesis and discussion of the outcomes related to generic prescribing. This made it difficult to interpret the extent of the impact of the intervention on generic drug use in some studies.

Only two reviews had a reasonable volume of primary studies reporting generic prescribing outcomes.[6, 7] The most informative review for our research question and the UK specific focus was a Cochrane review evaluating the effect of prescribing policies using financial incentives. [6] There was evidence across all the studies included in the review of an increase in generic prescribing with fundholding, though this was not statistically significant in all the studies. In the controlled before and after studies the increase ranged from 8.8% to 13.4% at 12 months and between 4% and 17.2% at 24 months. In one controlled interrupted time series there was a 15% increase in generic prescribing (range -43.7% to 190.5%) at 12 months; in a second study using the same design there was an 18.3% increase (range 13.6% to 23%). The authors reported that budgeting funds to a group of or individual physicians (i.e. giving them financial responsibility for their own budget) increased the use of generic drugs. [6] However, the majority of studies had serious limitations and the authors cautioned that the results should be interpreted with care.[6]

The second review with a strong focus on generic prescribing, which was less relevant to the UK NHS, focused on policy intervention in low and middle income countries. The review found insufficient evidence to determine which pro-generic policies increase utilisation of generic medicines in this setting.[7] The remainder of the reviews were more specific to the US healthcare system and less relevant to the UK NHS. In addition, six of the reviews contained only a single primary study reporting generic prescribing outcomes.[8-13] Overall, most of the interventions considered in the reviews showed an increase in generic prescribing.

Table 1: Included systematic reviews

Study details	Literature search end date	Summary of authors' objective	Intervention
Carroll (2003)[8]	09/2002	To evaluate whether community pharmacists have the ability to influence prescribing decisions and the extent to which they do so	Pharmacist interventions
Figueiras	1997	To propose effective continuing medical	Educational

(2001)[11]		education strategies to improve prescribing practices	strategies
Gibson (2005)[14]	04/2005	To determine whether patients respond to increased cost sharing by substituting less expensive alternatives for medications with higher levels of copayments or coinsurance	Cost-sharing
Green (2010)[12]	01/2009	To determine the effects of a pharmaceutical policy restricting the reimbursement of selected medications on drug use, health care utilization, health outcomes and costs	Policy restrictions on reimbursed drugs
Ivers (2012)[13]	09/2011	To investigate the effectiveness of audit and feedback to improve processes and outcomes of care and to examine factors that could influence intervention effectiveness	Audit and feedback
Kaplan (2012)[7]	01/2012	To inquire into the nature, extent and strength of the evidence for successful implementation of pro-generic medicines policies in low and middle income countries.	Pro-generic medicines policies
Mitchell (2001)[10]	1997	To appraise findings from studies examining the impact of computers on primary care consultations	Computer systems for use by doctors during consultations
McKibbon (2011)[9]	09/2009	To review the evidence on the impact of health information technology (IT) on all phases of the medication management process	IT used in the medication management process
Sturm (2007)[6]	08/2005	To determine the effects of prescribing policies using financial incentives for prescribers on drug use, healthcare utilisation, health outcomes and costs	Financial incentives (fundholding, drug budgets)

Rapid review of primary studies

A total of 11,690 records were identified from the searches of which 6144 records were potentially relevant for the rapid review (Figure 1). On the basis of screening title and abstracts, 99 full papers were ordered for further assessment. In addition, one paper was retrieved from hand searching, making a total of 100 full papers. Of the 100 full papers, 87 were excluded because; they did not meet the inclusion criteria, did not focus on generic prescribing or were irrelevant to the NHS. We also excluded studies of financial incentives as the main intervention as this had been adequately covered in a previous systematic review.[6] One study was unobtainable.[15]

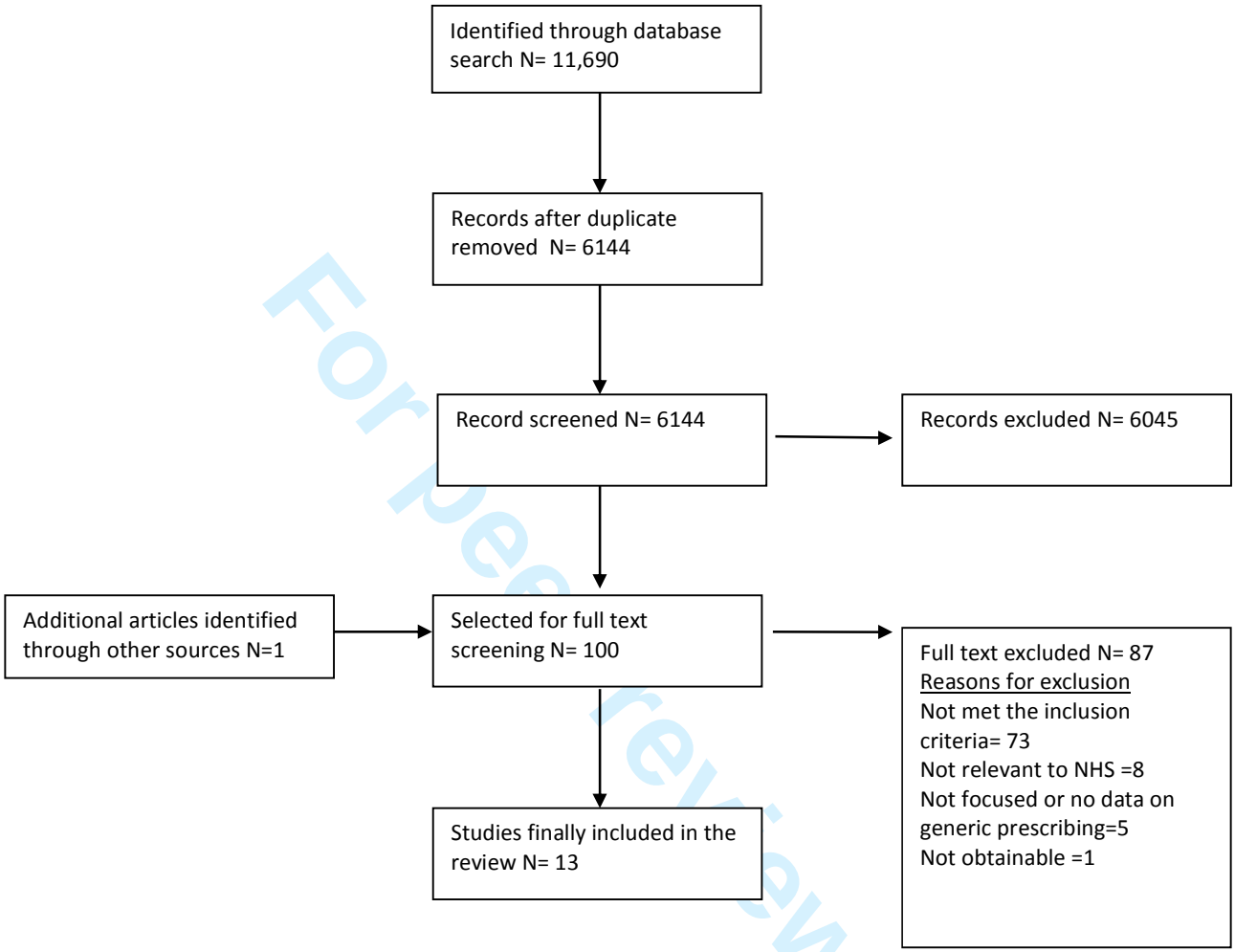

Figure 1: Study Flow Diagram

Intervention studies

Thirteen studies met the inclusion criteria: two RCTs (one individual and one cluster randomisation);[16, 17] nine CBA;[18-26] and two ITS (one with control group).[27, 28]

Most of the studies were in a primary care setting; five were conducted in the UK. [17, 21-24] The interventions were single or multi-component, and included professional educational interventions (2 studies), physicians' collaboration with pharmacists (2 studies), electronic prescribing (2 studies), and multi-faceted interventions which also included the above interventions as well as networking, feedback and financial incentives (7 studies). Most of the control groups used usual practice or no intervention. Where reported baseline generic prescribing rates ranged from 3.12% to 69.4% in the intervention groups and 16.2% to 82% in the control groups.

Risk of bias in included intervention studies

The risk of bias results are summarised in tables 2 and 3.

Table 2: Risk of bias for RCTs and CBA studies

	1	2	3	4	5	6	7	8	9
RCTs									
Braybrook (2000)[17]	UC	H	L	H	UC	UC	L	L	-
Meyer (2001)[16]	L	L	L	UC	UC	UC	L	L	H
CBA									
Fischer (2008)[20]	H	H	L	H	H	L	L	L	L
Geoghegan (1998)[21]	H	H	L	UC	UC	L	L	L	UC
Leach (1999)[22]	H	H	L	UC	UC	L	L	L	L
Mastura (2008)[19]	H	H	H	UC	UC	H	L	L	H
Niquille (2010)[26]	H	H	UC	UC.	UC	H	L	H	-
Onion (1998)[23]	H	H	L	UC	L	L	L	L	L
Walker (2002)[24]	H	H	H	H	UC	UC	L	L	-
Wensing (2004)[25]	H	H	L	UC	L	L	L	L	H
Wensing (2009)[18]	H	H	L	UC	L	L	L	L	-

Key: 1. Sequence generation; 2. Allocation concealment; 3. Baseline measurements; 4. Baseline characteristics; 5. incomplete outcome data; 6. Blinded assessment of primary outcome; 7. Protection against contamination; 8. Selective outcome reporting; 9. Other risk of bias
H=high, L=low, UC=unclear

Table 3: Risk of bias for ITS studies

	1	2	3	4	5	6	7
Lopez-Picazo Ferrer (2002)[28]	UC	L	L	L	UC	L	H
Stenner (2010) [27]	L	L	L	L	UC	L	-

Key: 1. Intervention independent of other changes; 2. Shape of intervention effect; 3. Intervention unlikely to affect data collection; 4. Knowledge of allocated intervention adequately prevented; 5. Incomplete outcome data; 6. Selective outcome reporting; 7. Other risk of bias.
H=high, L=low, UC=unclear

Table 4: Characteristics of intervention studies

Study details Country/setting	Populations	Intervention	Control
Cluster RCT			
Braybrook (2000)[17] UK/ Primary care	General medical practices contracted to Gwent Health Authority (September 1993 to March 2004)	Active feedback (N= 34 practices): Visits from pharmaceutical prescribing adviser to present prescribing analysis and cost (PACT) data concerning NSAID use and to promote prescribing review.	Passive feedback (N=32 practices): Practice specific prescribing analysis workbook containing similar information to the intervention. Reference group (N=22 practices): Received no information on NSAIDs from the prescribing adviser
RCT			
Meyer (2001) [16] South Africa/ Primary health care clinics	Primary health care nurses in the Northern Province of South Africa (1997)	4-day effective prescribing training workshops provided by 24 provincial trainers who had previously received a generic training-of-trainers course and one week effective prescribing course. The effective prescribing training used the WHO annual Guide to Good Prescribing as a framework and problem-based learning methods were used. N=12 primary health care clinics randomised (11 analysed)	No training N=12 primary health care clinics randomised (11 analysed)
CBA			

Fischer (2008)[20] USA/ Community-based practices	Clinicians from community-based practices from Massachusetts (2003- 2005)	E-prescription with FDS (formulary decision support); E-prescription system (Pocket Script) identifies preferred medications, often generic medications N=1198 clinicians (clinicians needed to write at least 1e-priscriptions)	Unenrolled prescribers (Clinicians who did not use e-prescription) N= 34453 clinicians
Geoghegan (1998)[21] UK/ Primary care	General practices(GP) in St Helens and Knowsley	Prescribing meetings (at least six meeting a year) held between local GPs and community pharmacists, with agenda determined by GPs and pharmacists N=8 practices	Practices not participating in meetings N=50 practices
Leach (1999)[22] UK/ Primary care	Pharmacists and GP (general practitioners) practices in Dudley health authority	Prescribing advice to local GP from community pharmacists who had received relevant additional training (each practice received 4 visits a year from their community pharmacist) N= 5 practices (11 partners)	All remaining GP practices from the same health authority N=58 practices (151 partners)
Mastura (2008)[19] Malaysia/ Health clinic	Medical officers from government health clinics in Negeri Sembilan (2004)	Group academic detailing N=5 medical officers (1 clinic, 1848 prescriptions)	No intervention N=4 medical officers (1 clinic, 1525 prescriptions)
Niquille (2010)[26] Switzerland/ Primary care	General practices in the Swiss Canton of Fribourg who were non-dispensing physicians (1999-2007)	Quality circles (N=6 circles; 6 pharmacists and 24 GPs) Groups were moderated by specifically trained pharmacists (intervention included networking, feedback, interdisciplinary continuing education).	No intervention (N= 79 to 753 GPs each year since 1999)

Onion (1998)[23] UK/ Primary care	General practitioners (GP) in Wirral Health Authority (1992-1993)	N=10 practices Based on Ford's motivational systems theory. Included financial incentive; standard setting for improvement; interactive education; agreed performance standards for cost savings and clinical audit	No intervention (N=10 practices)
Walker (2002)[24] UK/ Primary care	General Practitioners involved in a commissioning group pilot in Southern Derbyshire (1997 – 1999)	N=9 practices; 36 GPs Pharmaceutical adviser 1 day a week for a year. Intervention included practice comparison feedback, peer review meetings, and prescribing recommendations.	No intervention (N=9 practices; 44 GPs)
Wensing (2004)[25] Germany/ Primary care	Primary care doctors from the Sachsen-Anhalt region, mainly from single-handed practices (1996-1998)	Quality circles (N=10 circles; 90 GPs) Groups were moderated by specifically trained primary care physicians. Intervention included educational session and structured feedback on individual prescribing practices.	No intervention (N=87 GPs): Random sample of physicians in the same region
Wensing (2009)[18] Germany/ Primary care	Primary care physicians (GPs) from 3 regions (2001-2003)	Quality circles (N=152 circles; 1090 GPs) Nine meetings. Intervention included provision of evidence based information and repeated feedback on individual prescribing patterns).	No intervention (N=2090 GPs): Random sample of physicians in the same region
ITS			
Lopez-Picazo (2002)[28]	Primary care teams from four of the six health areas of	N=45 practices; 339 GPs Each individual received information about individual, team and health district prescribing	N/A

Spain/ Primary care	Murcia (1998-2000)	behaviour; regularly updated information on generic drugs; up to three clinical outreach sessions with each primary care team; and specific generic prescribing goals and financial incentives to achieve the goals.	
Stenner (2010)27 USA/ Vanderbilt Medical Group's outpatient clinics	Health care practitioners at a single medical centre, Vanderbilt University Medical Centre (VUMC) (2005-2008)	E prescribing system(Rx-Star) Changes were made to how medications were displayed on the current e-prescribing system; available generic formulations were displayed in a larger bolder font and were listed above brand name medications regardless of whether the practitioner searched for generic or brand name N=1.1 million electronic prescriptions from 2000 unique prescribers	Hand-written prescriptions that were filled at a single VUMC outpatient pharmacy (without e-prescribing, non Rx-Star) N=4456 randomly sampled prescriptions

NA=Not applicable

Narrative synthesis of intervention studies

Educational interventions

One CBA [19] and one RCT[16], both had methodological limitations, evaluated an educational interventions. There was a statistically significant increase in use of generic drugs for upper respiratory tract infection at three months follow-up in the RCT (p<0.05). [16] However, the authors reported that only 30 prescriptions per clinic were analysed retrospectively and it was unclear how they selected prescriptions for analysis. [16] In the CBA study, the proportion of prescriptions using the brand name reduced in the intervention group compared to control but there was a very strong baseline imbalance at baseline (Intervention: Pre 33.9%, Post 19%; Control: Pre 82%; post 88.1%).[19] Overall, these studies suggest that educational interventions may be able to increase generic prescribing rates but limitations in methodology and differences in setting, as well as the small number of studies, limit the conclusions that can be drawn from them.

Physicians' collaboration with pharmacists

Two CBA studies evaluated the effectiveness of pharmacists working with General Practitioners (GPs).[21, 22] There was some baseline imbalance in one study.[22] Both studies showed improvement in generic prescribing rates, though in one study this was not statistically significant (p=0.338)[21]. In the second study there was a mean increase over baseline in total generic prescribing in the intervention group compared with control: 9/1000 at 3 months (P > 0.05), 10/1000 at 6 months (P > 0.05), 35/1000 at 12 months (P <0.01).[22] The differing results of these two studies together with their relatively weak design provide limited evidence as to whether collaboration between physicians and pharmacists can improve generic prescribing rates.

Electronic prescribing (e-prescribing)

Two studies (one CBA and one ITS), conducted in the USA, reported the effect of an e-prescribing system which identified generic medications.[20, 27] The risk of bias was relatively low in the ITS study whereas in the CBA study there were slight baseline imbalances. Both studies reported an increase in generic prescribing with e-prescribing when compared to control. In the ITS the proportion of generic prescribing increased from baseline in the intervention group (pre 32% to post 50%) and also very slightly increased in the control group (pre 29% to post 31% of hand-written prescriptions). The proportion of generic prescribing was still higher in intervention group compared to control after two years post intervention (p<0.0001) and increased significantly in every speciality with e-prescribing (range 11.8% to 62.5%).[27]

Similarly, the CBA study reported that the e-prescription group increased their generic prescribing from baseline compared to control (absolute change 3.7% vs. 2.6%). After adjusting for baseline differences between prescribers and for changes over time e-prescription corresponded to a 3.3% increase in generic prescribing. [20]

However, the relevance of this evidence to the UK is uncertain given the differences between the US and UK health systems and the fact that e-prescribing systems are already widespread.

Multi-faceted interventions

Seven studies examined multi-component interventions;[17, 18, 23-26, 28] five CBA studies, one cluster RCT and one ITS.

In three studies (one cluster RCT and two CBA), a major component of the intervention was meetings between GPs and pharmacists who were giving regular feedback and prescribing recommendations.[17, 24, 26] All three studies had high or unclear risk of bias for most criteria. Two were conducted in the UK.[17, 24] One study reported no significant increase in the percentage of overall

generic drugs compared to control (p=0.17) [24] whereas the other two studies[17, 26] reported increases in generic prescribing in the intervention group. One CBA study reported that the intervention group was always higher than control for the five main cardiovascular classes of drugs for 3 years but the difference between the two groups reduced over time in each of the drug classes.[26] The cluster RCT study reported that active and passive feedback increased generic prescribing of (non-steroidal anti-inflammatory drugs (NSAIDs) compared to the reference group (pre and post differences in active, passive and reference group: 7%, 6%, and 4%). [17]

Two CBA studies, involving 90 and 1090 GPs from Germany, used quality circles which were moderated by primary care doctors and involved structured feedback on individual prescribing patterns and educational sessions.[18, 25] Both studies were high risk of bias in randomisation and allocation concealment and unclear risk in baseline characteristics. The 2009 study,[18] which involved 1090 GPs, reported no significant difference in prescribing generic drugs compared to control whereas the 2004 study,[25] which involved 90 GPs, reported significant increase in the percentage of generic prescribing in the intervention group (OR 1.10, 95%CI 1.08 to 1.13).

One CBA study which involved GPs from 10 practices from the UK used multiple interventions which included financial incentives, setting of standards for improvement, interactive education, agreed performance for cost savings and clinical audit.[23] The risk of bias was high for randomisation and allocation concealment, and unclear for baseline characteristics. The authors reported that the proportion of generic prescribing increased in the intervention group by 5% compared with the control (OR 1.22, 95% CI 1.18 to 1.28, p<0.0001). However, differences in the two groups started to decline after a further three months. [23]

Finally we included an ITS study which involved 339 family physicians from 45 primary care teams from Spain who received personalised information regarding prescribing behaviour, updated information cards on generic drugs and a letter, clinical outreach session with each primary care team, specific prescribing goal and financial incentives.[28] The risk of bias was low for most criteria, however it was unclear whether the interventions were independent of other changes. The study reported increased generic prescribing in the intervention group. The mean percentage of generic prescriptions for the 3 month period immediately before the intervention was 2.79% and for the 3 months immediately following the end of the intervention was 17.63%; absolute improvement was 14.84% and relative improvement was 15.27%.[28]

Discussions

Summary of main results

Our objective was to identify and summarise the research evidence on interventions aimed at improving generic prescribing rates. We took a two stage approach: first we identified and summarised existing synthesised evidence. Second, as little synthesised evidence is available, we conducted a rapid review of the primary literature on interventions to improve rates of generic prescribing.

Only two systematic reviews focused specifically on generic prescribing behaviours. The evidence from a Cochrane review suggests possible benefits of financial incentives to support generic prescribing.[6] Many areas currently use prescribing incentive schemes to support cost-effective prescribing and this strategy is endorsed, subject to suitable safeguards, by the English Department

of Health.[29] The second review with a strong focus on generic prescribing, which was less relevant to the NHS, focused on policy intervention in low and middle income countries.

We identified thirteen primary studies which evaluated the effects of an intervention to improve generic drug utilisation. Two studies evaluated an educational intervention and showed an increase in the percentage of overall prescribing of generic drugs; two studies which evaluated the effect of physicians collaborating with pharmacists showed improvement in generic prescribing rates, though in one study this was not statistically significant; and two studies from the USA which evaluated e-electronic prescribing showed improvements in generic prescribing. Seven studies used multi-component interventions. The interventions included various combinations of education, collaborations with pharmacists, quality circles, financial incentives and feedback on prescribing practices.

Five of the seven studies of multiple component interventions reported significant improvements in rates of generic prescribing associated with the intervention. However, only one of these was a randomised trial[17] and that trial was deemed to be at relatively high risk of bias. Similarly, two out of three studies with relatively similar interventions from the UK reported positive results, though one was not statistically significant.[17, 24] One study[23] differed from the others by incorporating financial incentives (which are considered possibly effective based on systematic review evidence) and by being based on a specific theory of behaviour change. A major limitation of these studies is that they were conducted between 1998 and 2002, so their relevance to the present-day NHS may be questionable. In addition, only five primary studies out of 13 were from the UK. Overall, the evidence on multiple component interventions, as with that for specific single interventions appears too weak and heterogeneous to provide clear guidance on how generic prescribing might be further improved.

Strengths and limitations of the review process

We searched several different databases for published as well as unpublished studies. The study quality was assessed systematically and taken into consideration in the synthesis. Appropriate methods were employed to minimise reviewer bias and error in all stages of the review process. We included only English-language studies for the rapid review, both for practical reasons related to the resources available, and because we were primarily interested in studies which are relevant to the UK NHS setting. While this might have led to the risk of relevant studies being overlooked, in practice the risk is likely to be small.

A feature of this project was the adoption of a two-stage approach, with an initial mapping of synthesised evidence followed by a review of primary studies guided by the results of the first stage. Examination of the available systematic reviews of interventions to improve prescribing allowed us to identify financial incentives as an intervention with a reasonable evidence base of research relevant to the UK NHS. This in turn reduced the work involved in the review of primary literature.

Limitations of the evidence base

Even though most interventions had positive results various methodological weaknesses especially in randomisation and allocation concealment may have biased their findings. Only two of the primary studies included in our rapid review were RCTs.[17] In addition most of the studies had small sample sizes. Most of the studies attracted participants who had expressed an interest in generic prescribing or who were already involved in fundholding; therefore, they have had increased motivation to save money by prescribing generic drugs which could overestimate the effects. In addition, the long term effects on generic prescribing were not reported, so it was unclear whether

the observed effects were sustainable in the longer run. However, it is arguable that studies reporting benefit up to 12 months suggest that the effects can be sustained.

Implications for policy and practice

Generic prescribing in the NHS is already at a high level and achievement of 100% generic prescribing is neither feasible nor desirable. However, variations between areas suggest that further improvement is still possible.

Evidence from a Cochrane systematic review suggests possible benefits of financial incentives to support generic prescribing.[6] The UK studies included in the review mainly relate to GP fundholding which is no longer used. Many areas use prescribing incentive schemes to support cost-effective prescribing.[29] Incentive schemes may focus on specific drugs or drug classes in accordance with local conditions.

The review of primary studies suggested that a range of interventions may be effective in increasing rates of generic prescribing. However, limitations in the evidence base make it difficult to identify any specific intervention or combination of interventions particularly suitable for implementation in the contemporary NHS setting. Decision-makers will need to consider which interventions appear most suitable to their specific setting. They may also want to consider whether the likely benefits of an intervention will outweigh its costs given the high levels of generic prescribing achieved by existing measures.

A number of systematic reviews of better quality evidence have shown modest absolute increases in desired health professional behaviours associated with interventions like audit and feedback, educational meetings and outreach and reminder systems.[13, 30] Given the relative consistency of results, this evidence in conjunction with our review findings could help in estimating the likely impact of a proposed intervention on generic prescribing behaviour.

Implications for research

Although high quality RCTs would improve the evidence base, it is unclear whether such studies would be justified, as the sample size required to demonstrate a benefit over current best practice would be large and the absolute improvement would be small. However, trials of specific interventions targeted at practices or individuals with particularly low levels of generic prescribing could be considered. Such trials should evaluate interventions that have proved successful in changing other types of behaviour and are based on a robust theory of behaviour change.

Given the existence of substantial variation between areas and individual general practices, further research may be helpful to explore the reasons for this. Research could focus on specific highly prescribed drugs with generic forms available (e.g. statins) and use a qualitative or mixed methods design.

Conclusions

Although several interventions look promising, complex interventions, methodological weaknesses and conflicting results limit the validity and applicability of the findings. In particular most of the available studies were conducted with baseline rates of generic prescribing significantly lower than the NHS is currently achieving. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

Funding: This work was supported by the NIHR CLAHRC for Leeds, York & Bradford.

Contributorship: MH designed the search strategy. TMB, DC and CMcD performed the literature search, screened the titles and abstracts and managed the references. All 3 reviewers (TMB, DC and CMcD) screened the retrieved papers against inclusion criteria and independently performed the data extraction and quality evaluation assessment for the review. All 3 reviewers interpreted the results. All authors have approved the manuscript and given approval for it to be published.

Data Sharing: Extra data can be accessed by e-mailing duncan.chambers@york.ac.uk

Competing Interests: None

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supp
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	-
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	-
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6-8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6,8,10-13
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6, 14-15
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	-
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14-15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	-
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

SUPPLEMENTARY

Search strategies for the rapid review of primary literature

Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Library, Wiley

http://onlinelibrary.wiley.com/

Issue 4 of 12, April 2013

Search date: 17th May 2103

Records retrieved: 188

ID	Search	Hits
#1	MeSH descriptor: [Physician's Practice Patterns] this term only	945
#2	MeSH descriptor: [Prescriptions] this term only	70
#3	MeSH descriptor: [Drug Prescriptions] this term only	417
#4	MeSH descriptor: [Electronic Prescribing] this term only	18
#5	MeSH descriptor: [Medical Order Entry Systems] this term only	49
#6	MeSH descriptor: [Medication Systems] this term only	24
#7	MeSH descriptor: [Medication Systems, Hospital] this term only	41
#8	(prescrib* or eprescrib*):ti,ab,kw	6610
#9	(prescription* or eprescription*):ti,ab,kw	3508
#10	dispens*:ti,ab,kw	788
#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	10382
#12	MeSH descriptor: [Drugs, Generic] this term only	199
#13	generic*:ti,ab,kw	1345
#14	(non next proprietary):ti,ab,kw	7
#15	#12 or #13 or #14	1352
#16	#11 and #15	109
#17	MeSH descriptor: [Drug Substitution] this term only	58
#18	(substitut* near/2 (generic* or (non next proprietary) or therapeutic*)):ti,ab,kw	74
#19	#17 or #18	131
#20	#16 or #19 from 1985 to 2013, in Trials	188

Key:

MeSH descriptor = indexing term (MeSH heading)

* = truncation

:ti,ab,kw = terms in either title or abstract or keyword fields

near/2 = terms within two word of each other (any order)

next = terms are next to each other

CINAHL via Ebsco

http://www.ebsco.com/

Inception – 10th May 2013

Search date: 17th May 2013

Records retrieved: 562

#	Query	Results
S24	S16 OR S22 Limiters - English Language; Published Date from: 19850101-20131231	562
S23	S16 OR S22	571
S22	S17 OR S18 OR S19 OR S20 OR S21	115
S21	TI substitut* N2 therapeutic* OR AB substitut* N2 therapeutic*	26
S20	TI substitut* N2 "non proprietary" OR AB substitut* N2 "non proprietary"	0
S19	TI substitut* N2 nonproprietary OR AB substitut* N2 nonproprietary	0
S18	TI substitut* N2 non-proprietary OR AB substitut* N2 non-proprietary	0
S17	TI substitut* N2 generic* OR AB substitut* N2 generic*	92
S16	S10 AND S15	506

S15	S11 OR S12 OR S13 OR S14	5,404
S14	TI "non proprietary" OR AB "non proprietary" OR TI non-proprietary OR AB non-proprietary	15
S13	TI nonproprietary OR AB nonproprietary	48
S12	TI generic* OR AB generic*	4,528
S11	(MH "Drugs, Generic")	1,568
S10	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9	38,541
S9	TI dispens* OR AB dispens*	2,059
S8	TI prescription* OR AB prescription* OR TI eprescription* OR AB eprescription*	12,270
S7	TI prescrib* OR AB prescrib* OR TI eprescrib* OR AB eprescrib*	18,772
S6	(MH "Practice Patterns")	3,932
S5	(MH "Medication Systems")	1,052
S4	(MH "Electronic Order Entry")	1,388
S3	(MH "Prescriptions, Drug")	3,752
S2	(MH "Prescriptive Authority")	3,771
S1	(MH "Prescribing Patterns")	1,488

Key:

MH = indexing term (CINAHL heading)

* = truncation

TI = words in the title

AB = words in the abstract

" " = phrase search

N2 = terms within two words of each other (any order)

EMBASE via OvidSP

http://ovidsp.ovid.com/

1980 to 2013 week 19

Searched on: 17th May 2013

Records retrieved: 4795

1 clinical practice/ (150206)

2 prescription/ (98358)

3 electronic prescribing/ (800)

4 computerized provider order entry/ (530)

5 (prescrib$ or eprescrib$).ti,ab. (114426)

6 (prescription$ or eprescription$).ti,ab. (75360)

7 dispens$.ti,ab. (29987)

8 or/1-7 (368968)

9 generic drug/ (7959)

10 generic$.ti,ab. (31529)

11 non-proprietary.ti,ab. (171)

12 nonproprietary.ti,ab. (234)

13 or/9-12 (35545)

14 8 and 13 (4900)

15 *drug substitution/ (335)

16 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (1055)

17 15 or 16 (1316)

18 14 or 17 (5722)

19 animal/ (1816382)

20 exp animal experiment/ (1584117)

21 Nonhuman/ (4050841)

22 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh. (4570661)

23 19 or 20 or 21 or 22 (6577334)

24 exp human/ (14329978)

25 human experiment/ (311984)

26 24 or 25 (14331371)

27 23 not (23 and 26) (5088908)

28 18 not 27 (5632)

29 limit 28 to yr="1985 -Current" (5494)

30 limit 29 to english language (4795)

Key:

/ = indexing term (EMTREE heading)

exp = exploded EMTREE heading

* = focussed EMTREE heading

$ = truncation

.ti,ab. = terms in either title or abstract fields

sh = terms in the subject heading field

adj2 = terms within two words of each other (any order)

Health Management Information Consortium via OvidSP

http://ovidsp.ovid.com/

1979 to March 2013

Searched on: 17th May 2013

Records retrieved: 228

1 exp prescribing/ (3145)

2 exp prescribing costs/ (143)

3 exp prescriptions/ (631)

4 prescription charges/ or prescription drugs/ or prescription pricing authority/ (688)

5 exp drug dispensing/ (407)

6 exp medication systems/ (37)

7 (prescrib$ or eprescrib$).ti,ab. (4632)

8 (prescription$ or eprescription$).ti,ab. (2856)

9 dispens$.ti,ab. (921)

10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (8446)

11 generic drugs/ (99)

12 generic$.ti,ab. (1263)

13 non-proprietary.ti,ab. (1)

14 nonproprietary.ti,ab. (10)

15 11 or 12 or 13 or 14 (1287)

16 10 and 15 (223)

17 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (34)

18 16 or 17 (232)

19 limit 18 to yr="1985 -Current" (228)

20 limit 19 to english (228)

Key:

/ = indexing term

exp = exploded indexing term

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

MEDLINE In-Process & Other Non-Indexed Citations and MEDLINE via OvidSP
http://ovidsp.ovid.com/

1946 to 16th May 2013

Searched on: 17th May 2013

Records retrieved: 2700

1 Physician's Practice Patterns/ (38329)

2 Prescriptions/ (1760)

3 Drug Prescriptions/ (21281)

4 Electronic Prescribing/ (451)

5 Medical Order Entry Systems/ (1318)

6 Medication Systems/ (722)

7 Medication Systems, Hospital/ (3103)

8 (prescrib$ or eprescrib$).ti,ab. (81556)

9 (prescription$ or eprescription$).ti,ab. (52201)

10 dispens$.ti,ab. (24461)

11 or/1-10 (180883)

12 Drugs, Generic/ (3329)

13 generic$.ti,ab. (26385)

14 non-proprietary.ti,ab. (125)

15 nonproprietary.ti,ab. (179)

16 or/12-15 (27814)

17 11 and 16 (2230)

18 Drug Substitution/ (665)

19 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (660)

20 17 or 18 or 19 (3233)

21 exp animals/ not humans/ (3847816)

22 20 not 21 (3206)

23 limit 22 to yr="1985 -Current" (3056)

24 limit 23 to english language (2700)

Key:

/ = indexing term (MeSH heading)

exp = exploded MeSH heading

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

PsycINFO via OvidSP

http://ovidsp.ovid.com/

1806 to May week 2 2013

Searched on: 17th May 2013

Records retrieved: 354

1 exp "prescribing (drugs)"/ (2629)

2 prescription drugs/ (2248)

3 (prescrib$ or eprescrib$).ti,ab. (19193)

4 (prescription$ or eprescription$).ti,ab. (12067)

5 dispens$.ti,ab. (2312)

6 1 or 2 or 3 or 4 or 5 (30538)

7 generic drugs/ (93)

8 generic$.ti,ab. (8365)

9 non-proprietary.ti,ab. (11)

10 nonproprietary.ti,ab. (20)

11 7 or 8 or 9 or 10 (8396)

12 6 and 11 (347)

13 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (84)

14 12 or 13 (384)

15 limit 14 to yr="1985 -Current" (375)

16 limit 15 to english language (354)

Key:

/ = indexing term

exp = exploded indexing term

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

PubMed

http://www.ncbi.nlm.nih.gov/pubmed

Searched on: 17th May 2013

Records retrieved: 2863

Search	Query	Items found
#56	Search #34 OR #36 OR #48 Filters: Publication date from 1985/01/01 to 2013/12/31; English Sort by: PublicationDate	2863
#53	Search #34 OR #36 OR #48 Filters: Publication date from 1985/01/01 to 2013/12/31	3222
#52	Search #34 OR #36 OR #48	3361
#48	Search (generic*[Title/Abstract]) AND substitut*[Title/Abstract]	928
#36	Search "Drug Substitution"[Mesh]	629
#34	Search #26 AND #33	2216
#33	Search #28 OR #29 OR #30	27833
#30	Search ((non-proprietary[Title/Abstract]) OR nonproprietary[Title/Abstract]) OR "non proprietary"[Title/Abstract]	296
#29	Search generic*[Title/Abstract]	26428
#28	Search "Drugs, Generic"[Mesh]	3273
#26	Search #7 OR #10 OR #13 OR #15 OR #17 OR #20 OR #22 OR #23 OR #24 OR #25	179712
#25	Search dispens*[Title/Abstract]	23786
#24	Search (prescription*[Title/Abstract]) OR eprescription*[Title/Abstract])	52177
#23	Search (prescrib*[Title/Abstract]) OR eprescrib*[Title/Abstract]	81730
#22	Search "Medication Systems, Hospital"[Mesh]	3070
#20	Search "Medication Systems"[Mesh:NoExp]	709

Search	Query	Items found
#17	Search "Medical Order Entry Systems"[Mesh]	1281
#15	Search "Electronic Prescribing"[Mesh]	431
#13	Search "Drug Prescriptions"[Mesh:NoExp]	20964
#10	Search "Prescriptions"[Mesh:NoExp]	1732
#7	Search "Physician's Practice Patterns"[Mesh]	37546

Key:

[Mesh] = exploded indexing term (MeSH heading)

[Mesh:NoExp] = indexing term (MeSH heading) not exploded

* = truncation

[Title/Abstract]) = terms in either title or abstract

BMJ Open

Behaviour changes interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004623.R1
Article Type:	Research
Date Submitted by the Author:	26-Mar-2014
Complete List of Authors:	Moe-Byrne, Thirimon; University of York, Centre for reviews and dissemination Chambers, Duncan; University of York, Centre for reviews and dissemination Harden, Melissa; University of York, Centre for reviews and dissemination McDaid, Catriona; University of York, York Trials Unit
Primary Subject Heading:	Pharmacology and therapeutics
Secondary Subject Heading:	General practice / Family practice
Keywords:	PRIMARY CARE, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Title: Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review

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Abstract: 299 words

Full text: 3725 words

Number of figures: 1

Number of tables: 4

Keywords: Generic prescribing, Primary care, General practice, Health policy, Organisation of health services

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ABSTRACT

Objective: To summarise evidence on the effectiveness of behaviour change interventions to encourage prescribing of generic forms of prescription drugs where clinically appropriate in the UK NHS and similar settings.

Design: systematic review

Search strategy: We conducted a rapid evidence synthesis in two stages: Firstly, we searched databases such as the Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE), for systematic reviews of interventions that reported outcomes related to utilisation of generic drugs. For the second stage, we searched several databases including MEDLINE and EMBASE to identify primary studies of any interventions not adequately covered by systematic reviews.

Data extraction and quality assessment: Data were extracted into a standardised data extraction form. Standardised quality assessment tools were used to assess study quality. Two reviewers were involved in data extraction and quality assessment.

Results: Ten reviews were included for the initial evidence synthesis but most were of limited usefulness to our focused review question. One review evaluated the effect of prescribing policies using financial incentives and showed an increase in generic prescribing. Thirteen primary studies of other interventions were included for the rapid review. Two studies showed an increase in percentage of overall generic prescribing with an educational intervention; two studies showed improvement in generic prescribing rates when physicians collaborated with pharmacists, though in one study this was not statistically significant; two US studies showed improvements in generic prescribing with electronic prescribing. Five out of seven studies showed positive results with multi-faceted interventions.

Conclusions: The existing evidence remains insufficient to determine which behaviour change intervention or combination of interventions is most effective due to methodological weaknesses and conflicting results. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

Article Summary

'Strengths and limitations of this study'

- Appropriate use of generic medicines is important for healthcare systems to make optimum use of limited resources. In England, rates of prescribing by generic name are over 80% overall but there is evidence of variation between regions and individual prescribers.
- We have synthesised evidence from systematic and primary studies that have evaluated the effectiveness of interventions to promote generic prescribing at the level of the individual prescriber or GP practice.
- The study brings together evidence on a wide range of behaviour change interventions and identifies a number of potentially effective approaches.
- Limitations of the evidence base make it difficult to draw any firm conclusions about the relative effectiveness of different approaches. Recent evidence from UK NHS settings is particularly lacking.
- Given the uncertainty around the evidence base, decision-makers in settings where only small improvements in generic prescribing rates are likely to be achievable should take into account the practicality and costs of the intervention before implementing measures designed to further increase generic prescribing rates.

BACKGROUND

Generic medicines, which are the substitutes of original (branded) medicines with the same quality, safety and efficacy,[1] offer an interesting opportunity for governments and healthcare payers to contain escalating healthcare budgets as their prices tend to be 10–80% lower than their proprietary equivalents.[2] In England the proportion of prescriptions prescribed generically (i.e. by non-proprietary name rather than brand name) increased from 76% in 2002 to 83.6% in 2012.[3]

Despite the trend of increasing generic prescribing rates there is thought to be room for greater efficiency. In 2008 approximately 5% of medicines were prescribed by their brand name in England when there was a generic alternative available.[4] A national Audit Office report in 2007 reported that prescriptions of generic statins (simvastatin and pravastatin) varied from 28% to 86% across English Primary Care Trusts.[5] More recent research has also identified marked variation in generic prescribing by GPs (for data on statin prescriptions in England, see www.prescribinganalytics.com).

In 2009, the Department of Health consulted on a proposal for the introduction of generic substitution (allowing pharmacists to fulfil a prescription for a branded medicine by dispensing a generic equivalent) in primary care in England. However, after considering the responses to the consultation, the Government decided not to progress the proposal further.[4] As an alternative it was suggested that 'other, less nationally prescriptive mechanisms for further supporting the use of generic medicines can be explored'.

We have undertaken a rapid evidence synthesis to inform decision-makers about the evidence base for interventions that might be applied to increase generic prescribing at the level of the individual or small units such as general practices.

Aims/objectives

To identify and summarise relevant research evidence using existing synthesised evidence sources (systematic reviews) supplemented as necessary by a rapid systematic review of primary research. The project aims to benefit the UK NHS by increasing the accessibility of the relevant evidence and by identifying gaps that need to be filled by further research.

Methods

We conducted this rapid evidence synthesis in two stages: an initial mapping of existing sources of synthesised evidence followed by rapid systematic review of the primary research literature, for interventions not covered by previous reviews. We registered the protocol of this review on PROSPERO the international prospective register of systematic reviews (registration number CRD42013004443).

Mapping of synthesised evidence

We searched the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment (HTA) database and Health Systems Evidence for the systematic reviews to map the existing sources of synthesised evidence. Terms relating to prescribing were combined using the Boolean operator AND with terms for generic drugs. No date or language limits were applied.

Systematic reviews, HTA reports and overviews were included if they evaluated the effectiveness or efficacy of an intervention and reported an outcome or outcomes related to utilisation (prescribing or dispensing) of generic drugs regardless of indication, setting or type of healthcare system. One reviewer examined the search results to identify potentially relevant reports. Full texts of potentially relevant reports were assessed for inclusion by two reviewers independently. Any disagreements were resolved by discussion and if necessary by involving a third reviewer.

Essential details of included reports were extracted using a simple data extraction form. These included the stated objectives, inclusion criteria, period covered by the search, interventions in included studies, main results and authors' conclusions. Data were extracted by one reviewer and checked by a second. The results were synthesised narratively and used to guide searching of the primary literature. In particular, interventions considered to be adequately covered by existing synthesised evidence were excluded from the rapid review of primary literature.

Rapid review of primary literature

Selection of studies

For the second stage, the previous search strategy described above was adapted for use in databases containing primary studies. We searched PubMed, MEDLINE, MEDLINE In-Process, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index of Nursing and Allied Health (CINAHL), EMBASE, Health Management Information Consortium (HMIC) and PsycINFO for studies published in English language during the period between 1985 and May 2013 (see supplementary).

Primary studies evaluating interventions designed to promote prescribing and/or dispensing of generic drugs were included. The main focus was interventions applied to individuals but interventions at the group (e.g. general practice) level were also eligible. Studies which looked at financial incentives as a main intervention were excluded as there were already reviews covering those aspects in generic prescribing. We excluded interventions considered not applicable in UK NHS settings and also generic substitution because the Department of Health decided after a consultation exercise not to introduce such a policy. Randomised or quasi-randomised controlled trials, controlled before-and-after (CBA) studies and interrupted time-series (ITS), based on Cochrane EPOC (Effective Practice and Organisation of Care) Group definitions, were eligible. The primary outcome was any measure of rate of prescribing or dispensing of generic drugs (relative to comparator group or change over time). Studies of barriers and facilitators of generic prescribing were also included but this will be reported elsewhere (a full report is available from the authors).

Records were initially screened by one reviewer to remove obviously irrelevant material, the remaining records and full papers were screened independently by two reviewers. Any disagreements were discussed with a third reviewer.

Data extraction and quality assessment

Data on objectives, setting, study design, participants, details of the intervention(s) and results/conclusions related to rates of generic prescribing/dispensing were extracted. Risk of bias was assessed using the criteria of the Cochrane EPOC Group. This was undertaken by one reviewer and checked by a second; disagreements were resolved by discussion.

Methods of synthesis

The substantial heterogeneity of interventions and method across studies precluded meta-analysis and we therefore reported in a narrative synthesis. Studies were grouped by type of intervention or interventions.

Results

Mapping of synthesised evidence

The search identified 356 potentially relevant references: 40 full papers were ordered; 10 systematic reviews (9 reviews and one overview of reviews) which evaluated interventions such as financial incentives, prescribing policies, cost sharing, use of computers/IT, educational interventions, audit and feedback (Table 1).

Most of the reviews had broad objectives and did not focus specifically on interventions targeted at increasing rates of generic prescribing, for example they looked at prescribing behaviour in general rather than specifically generic prescribing. As a result there was often limited synthesis and discussion of the outcomes related to generic prescribing. This made it difficult to interpret the extent of the impact of the intervention on generic drug use in some studies.

Only two reviews had a reasonable volume of primary studies reporting generic prescribing outcomes.[6, 7] The most informative review for our research question and the UK specific focus was a Cochrane review evaluating the effect of prescribing policies using financial incentives. [6] There was evidence across all the studies included in the review of an increase in generic prescribing with fundholding, though this was not statistically significant in all the studies. In the controlled before and after studies the increase ranged from 8.8% to 13.4% at 12 months and between 4% and 17.2% at 24 months. In one controlled interrupted time series there was a 15% increase in generic prescribing (range -43.7% to 190.5%) at 12 months; in a second study using the same design there was an 18.3% increase (range 13.6% to 23%). The authors reported that budgeting funds to a group of or individual physicians (i.e. giving them financial responsibility for their own budget) increased the use of generic drugs. [6] However, the majority of studies had serious limitations and the authors cautioned that the results should be interpreted with care.[6]

The second review with a strong focus on generic prescribing, which was less relevant to the UK NHS, focused on policy intervention in low and middle income countries. The review found insufficient evidence to determine which pro-generic policies increase utilisation of generic medicines in this setting.[7] The remainder of the reviews were more specific to the US healthcare system and less relevant to the UK NHS. In addition, six of the reviews contained only a single primary study reporting generic prescribing outcomes.[8-13] Overall, most of the interventions considered in the reviews showed an increase in generic prescribing.

Table 1: Included systematic reviews

Study details	Literature search end date	Summary of authors' objective	Intervention
Carroll (2003)[8]	09/2002	To evaluate whether community pharmacists have the ability to influence prescribing decisions and the extent to which they do so	Pharmacist interventions
Figueiras (2001)[11]	1997	To propose effective continuing medical education strategies to improve prescribing practices	Educational strategies

Gibson (2005)[14]	04/2005	To determine whether patients respond to increased cost sharing by substituting less expensive alternatives for medications with higher levels of copayments or coinsurance	Cost-sharing
Green (2010)[12]	01/2009	To determine the effects of a pharmaceutical policy restricting the reimbursement of selected medications on drug use, health care utilization, health outcomes and costs	Policy restrictions on reimbursed drugs
Ivers (2012)[13]	09/2011	To investigate the effectiveness of audit and feedback to improve processes and outcomes of care and to examine factors that could influence intervention effectiveness	Audit and feedback
Kaplan (2012)[7]	01/2012	To inquire into the nature, extent and strength of the evidence for successful implementation of pro-generic medicines policies in low and middle income countries.	Pro-generic medicines policies
Mitchell (2001)[10]	1997	To appraise findings from studies examining the impact of computers on primary care consultations	Computer systems for use by doctors during consultations
McKibbon (2011)[9]	09/2009	To review the evidence on the impact of health information technology (IT) on all phases of the medication management process	IT used in the medication management process
Sturm (2007)[6]	08/2005	To determine the effects of prescribing policies using financial incentives for prescribers on drug use, healthcare utilisation, health outcomes and costs	Financial incentives (fundholding, drug budgets)

Rapid review of primary studies

A total of 11,690 records were identified from the searches of which 6144 records were potentially relevant for the rapid review (Figure 1). On the basis of screening title and abstracts, 99 full papers were ordered for further assessment. In addition, one paper was retrieved from hand searching, making a total of 100 full papers. Of the 100 full papers, 87 were excluded because; they did not meet the inclusion criteria, did not focus on generic prescribing or were irrelevant to the NHS. We also excluded studies of financial incentives as the main intervention as this had been adequately covered in a previous systematic review.[6] One study was unobtainable.[15]

Figure 1: Study Flow Diagram

Intervention studies

Thirteen studies met the inclusion criteria: two RCTs (one individual and one cluster randomisation);[16, 17] nine CBA;[18-26] and two ITS (one with control group).[27, 28]

Most of the studies were in a primary care setting; five were conducted in the UK.[17, 21-24] The interventions were single or multi-component, and included professional educational interventions (2 studies), physicians' collaboration with pharmacists (2 studies), electronic prescribing (2 studies), and multi-faceted interventions which also included the above interventions as well as networking, feedback and financial incentives (7 studies). Most of the control groups used usual practice or no intervention. Where reported baseline generic prescribing rates ranged from 3.12% to 69.4% in the intervention groups and 16.2% to 82% in the control groups.

Risk of bias in included intervention studies

The risk of bias results are summarised in tables 2 and 3.

Table 2: Risk of bias for RCTs and CBA studies

	1	2	3	4	5	6	7	8	9
RCTs									
Braybrook (2000)[17]	UC	H	L	H	UC	UC	L	L	-
Meyer (2001)[16]	L	L	L	UC	UC	UC	L	L	H
CBA									
Fischer (2008)[20]	H	H	L	H	H	L	L	L	L
Geoghegan (1998)[21]	H	H	L	UC	UC	L	L	L	UC
Leach (1999)[22]	H	H	L	UC	UC	L	L	L	L
Mastura (2008)[19]	H	H	H	UC	UC	H	L	L	H
Niquille (2010)[26]	H	H	UC	UC.	UC	H	L	H	-
Onion (1998)[23]	H	H	L	UC	L	L	L	L	L
Walker (2002)[24]	H	H	H	H	UC	UC	L	L	-
Wensing (2004)[25]	H	H	L	UC	L	L	L	L	H
Wensing (2009)[18]	H	H	L	UC	L	L	L	L	-

Key: 1. Sequence generation; 2. Allocation concealment; 3. Baseline measurements; 4. Baseline characteristics; 5. incomplete outcome data; 6. Blinded assessment of primary outcome; 7. Protection against contamination; 8. Selective outcome reporting; 9. Other risk of bias
H=high, L=low, UC=unclear

Table 3: Risk of bias for ITS studies

	1	2	3	4	5	6	7
Lopez-Picazo Ferrer (2002)[28]	UC	L	L	L	UC	L	H
Stenner (2010) [27]	L	L	L	L	UC	L	-

Key: 1. Intervention independent of other changes; 2. Shape of intervention effect; 3. Intervention unlikely to affect data collection; 4. Knowledge of allocated intervention adequately prevented; 5. Incomplete outcome data; 6. Selective outcome reporting; 7. Other risk of bias.
H=high, L=low, UC=unclear

Table 4: Characteristics of intervention studies

Study details Country/setting	Populations	Intervention	Control
Cluster RCT			
Braybrook (2000)[17] UK/ Primary care	General medical practices contracted to Gwent Health Authority (September 1993 to March 2004)	Active feedback (N= 34 practices): Visits from pharmaceutical prescribing adviser to present prescribing analysis and cost (PACT) data concerning NSAID use and to promote prescribing review.	Passive feedback (N=32 practices): Practice specific prescribing analysis workbook containing similar information to the intervention. Reference group (N=22 practices): Received no information on NSAIDs from the prescribing adviser
RCT			
Meyer (2001) [16] South Africa/ Primary health care clinics	Primary health care nurses in the Northern Province of South Africa (1997)	4-day effective prescribing training workshops provided by 24 provincial trainers who had previously received a generic training-of-trainers course and one week effective prescribing course. The effective prescribing training used the WHO annual Guide to Good Prescribing as a framework and problem-based learning methods were used. N=12 primary health care clinics randomised (11 analysed)	No training N=12 primary health care clinics randomised (11 analysed)
CBA			

Fischer (2008)[20] USA/ Community-based practices	Clinicians from community-based practices from Massachusetts (2003- 2005)	E-prescription with FDS (formulary decision support); E-prescription system (Pocket Script) identifies preferred medications, often generic medications N=1198 clinicians (clinicians needed to write at least 1e-priscriptions)	Unenrolled prescribers (Clinicians who did not use e-prescription) N= 34453 clinicians
Geoghegan (1998)[21] UK/ Primary care	General practices(GP) in St Helens and Knowsley	Prescribing meetings (at least six meeting a year) held between local GPs and community pharmacists, with agenda determined by GPs and pharmacists N=8 practices	Practices not participating in meetings N=50 practices
Leach (1999)[22] UK/ Primary care	Pharmacists and GP (general practitioners) practices in Dudley health authority	Prescribing advice to local GP from community pharmacists who had received relevant additional training (each practice received 4 visits a year from their community pharmacist) N= 5 practices (11 partners)	All remaining GP practices from the same health authority N=58 practices (151 partners)
Mastura (2008)[19] Malaysia/ Health clinic	Medical officers from government health clinics in Negeri Sembilan (2004)	Group academic detailing N=5 medical officers (1 clinic, 1848 prescriptions)	No intervention N=4 medical officers (1 clinic, 1525 prescriptions)
Niquille (2010)[26] Switzerland/ Primary care	General practices in the Swiss Canton of Fribourg who were non-dispensing physicians (1999-2007)	Quality circles (N=6 circles; 6 pharmacists and 24 GPs) Groups were moderated by specifically trained pharmacists (intervention included networking, feedback, interdisciplinary continuing education).	No intervention (N= 79 to 753 GPs each year since 1999)

Onion (1998)[23] UK/ Primary care	General practitioners (GP) in Wirral Health Authority (1992-1993)	N=10 practices Based on Ford's motivational systems theory. Included financial incentive; standard setting for improvement; interactive education; agreed performance standards for cost savings and clinical audit	No intervention (N=10 practices)
Walker (2002)[24] UK/ Primary care	General Practitioners involved in a commissioning group pilot in Southern Derbyshire (1997 – 1999)	N=9 practices; 36 GPs Pharmaceutical adviser 1 day a week for a year. Intervention included practice comparison feedback, peer review meetings, and prescribing recommendations.	No intervention (N=9 practices; 44 GPs)
Wensing (2004)[25] Germany/ Primary care	Primary care doctors from the Sachsen-Anhalt region, mainly from single-handed practices (1996-1998)	Quality circles (N=10 circles; 90 GPs) Groups were moderated by specifically trained primary care physicians. Intervention included educational session and structured feedback on individual prescribing practices.	No intervention (N=87 GPs): Random sample of physicians in the same region
Wensing (2009)[18] Germany/ Primary care	Primary care physicians (GPs) from 3 regions (2001-2003)	Quality circles (N=152 circles; 1090 GPs) Nine meetings. Intervention included provision of evidence based information and repeated feedback on individual prescribing patterns).	No intervention (N=2090 GPs): Random sample of physicians in the same region
ITS			
Lopez-Picazo (2002)[28]	Primary care teams from four of the six health areas of	N=45 practices; 339 GPs Each individual received information about individual, team and health district prescribing	N/A

Spain/ Primary care	Murcia (1998-2000)	behaviour; regularly updated information on generic drugs; up to three clinical outreach sessions with each primary care team; and specific generic prescribing goals and financial incentives to achieve the goals.	
Stenner (2010)27 USA/ Vanderbilt Medical Group's outpatient clinics	Health care practitioners at a single medical centre, Vanderbilt University Medical Centre (VUMC) (2005-2008)	E prescribing system(Rx-Star) Changes were made to how medications were displayed on the current e-prescribing system; available generic formulations were displayed in a larger bolder font and were listed above brand name medications regardless of whether the practitioner searched for generic or brand name N=1.1 million electronic prescriptions from 2000 unique prescribers	Hand-written prescriptions that were filled at a single VUMC outpatient pharmacy (without e-prescribing, non Rx-Star) N=4456 randomly sampled prescriptions

NA=Not applicable

Narrative synthesis of intervention studies

Educational interventions

One CBA [19] and one RCT[16], both had methodological limitations, evaluated an educational interventions. There was a statistically significant increase in use of generic drugs for upper respiratory tract infection at three months follow-up in the RCT (p<0.05). [16] However, the authors reported that only 30 prescriptions per clinic were analysed retrospectively and it was unclear how they selected prescriptions for analysis. [16] In the CBA study, the proportion of prescriptions using the brand name reduced in the intervention group compared to control but there was a very strong imbalance at baseline (Intervention: Pre 33.9%, Post 19%; Control: Pre 82%; post 88.1%).[19] Overall, these studies suggest that educational interventions may be able to increase generic prescribing rates but limitations in methodology and differences in setting, as well as the small number of studies, limit the conclusions that can be drawn from them.

Physicians' collaboration with pharmacists

Two CBA studies evaluated the effectiveness of pharmacists working with General Practitioners (GPs).[21, 22] There was some baseline imbalance in one study.[22] Both studies showed improvement in generic prescribing rates, though in one study this was not statistically significant (p=0.338)[21]. In the second study there was a mean increase over baseline in total generic prescribing in the intervention group compared with control: 9/1000 at 3 months (P > 0.05), 10/1000 at 6 months (P > 0.05), 35/1000 at 12 months (P <0.01).[22] The differing results of these two studies together with their relatively weak design provide limited evidence as to whether collaboration between physicians and pharmacists can improve generic prescribing rates.

Electronic prescribing (e-prescribing)

Two studies (one CBA and one ITS), conducted in the USA, reported the effect of an e-prescribing system which identified generic medications.[20, 27] The risk of bias was relatively low in the ITS study whereas in the CBA study there were slight baseline imbalances. Both studies reported an increase in generic prescribing with e-prescribing when compared to control. In the ITS the proportion of generic prescribing increased from baseline in the intervention group (pre 32% to post 50%) and also very slightly increased in the control group (pre 29% to post 31% of hand-written prescriptions). The proportion of generic prescribing was still higher in intervention group compared to control after two years post intervention (p<0.0001) and increased significantly in every speciality with e-prescribing (range 11.8% to 62.5%).[27]

Similarly, the CBA study reported that the e-prescription group increased their generic prescribing from baseline compared to control (absolute change 3.7% vs. 2.6%). After adjusting for baseline differences between prescribers and for changes over time e-prescription corresponded to a 3.3% increase in generic prescribing. [20]

However, the relevance of this evidence to the UK is uncertain given the differences between the US and UK health systems and the fact that e-prescribing systems are already widespread.

Multi-faceted interventions

Seven studies examined multi-component interventions;[17, 18, 23-26, 28] five CBA studies, one cluster RCT and one ITS.

In three studies (one cluster RCT and two CBA), a major component of the intervention was meetings between GPs and pharmacists who were giving regular feedback and prescribing recommendations.[17, 24, 26] All three studies had high or unclear risk of bias for most criteria. Two were conducted in the UK.[17, 24] One study reported no significant increase in the percentage of overall

generic drugs compared to control (p=0.17) [24] whereas the other two studies[17, 26] reported increases in generic prescribing in the intervention group. One CBA study reported that the intervention group was always higher than control for the five main cardiovascular classes of drugs for 3 years but the difference between the two groups reduced over time in each of the drug classes.[26] The cluster RCT study reported that active and passive feedback increased generic prescribing of (non-steroidal anti-inflammatory drugs (NSAIDs) compared to the reference group (pre and post differences in active, passive and reference group: 7%, 6%, and 4%). [17]

Two CBA studies, involving 90 and 1090 GPs from Germany, used quality circles which were moderated by primary care doctors and involved structured feedback on individual prescribing patterns and educational sessions.[18, 25] Both studies were high risk of bias in randomisation and allocation concealment and unclear risk in baseline characteristics. The 2009 study,[18] which involved 1090 GPs, reported no significant difference in prescribing generic drugs compared to control whereas the 2004 study,[25] which involved 90 GPs, reported significant increase in the percentage of generic prescribing in the intervention group (OR 1.10, 95%CI 1.08 to 1.13).

One CBA study which involved GPs from 10 practices from the UK used multiple interventions which included financial incentives, setting of standards for improvement, interactive education, agreed performance for cost savings and clinical audit.[23] The risk of bias was high for randomisation and allocation concealment, and unclear for baseline characteristics. The authors reported that the proportion of generic prescribing increased in the intervention group by 5% compared with the control (OR 1.22, 95% CI 1.18 to 1.28, p<0.0001). However, differences in the two groups started to decline after a further three months. [23]

Finally we included an ITS study which involved 339 family physicians from 45 primary care teams from Spain who received personalised information regarding prescribing behaviour, updated information cards on generic drugs and a letter, clinical outreach session with each primary care team, specific prescribing goal and financial incentives.[28] The risk of bias was low for most criteria, however it was unclear whether the interventions were independent of other changes. The study reported increased generic prescribing in the intervention group. The mean percentage of generic prescriptions for the 3 month period immediately before the intervention was 2.79% and for the 3 months immediately following the end of the intervention was 17.63%; absolute improvement was 14.84% and relative improvement was 15.27%.[28]

Discussion

Summary of main results

Our objective was to identify and summarise the research evidence on interventions aimed at improving generic prescribing rates. We took a two stage approach: first we identified and summarised existing synthesised evidence. Second, as little synthesised evidence is available, we conducted a rapid review of the primary literature on interventions to improve rates of generic prescribing.

Only two systematic reviews focused specifically on generic prescribing behaviours. The evidence from a Cochrane review suggests possible benefits of financial incentives to support generic prescribing.[6] Many areas currently use prescribing incentive schemes to support cost-effective prescribing and this strategy is endorsed, subject to suitable safeguards, by the English Department

of Health.[29] The second review with a strong focus on generic prescribing, which was less relevant to the NHS, focused on policy intervention in low and middle income countries.

We identified thirteen primary studies which evaluated the effects of an intervention to improve generic drug utilisation. Two studies evaluated an educational intervention and showed an increase in the percentage of overall prescribing of generic drugs; two studies which evaluated the effect of physicians collaborating with pharmacists showed improvement in generic prescribing rates, though in one study this was not statistically significant; and two studies from the USA which evaluated e-electronic prescribing showed improvements in generic prescribing. Seven studies used multi-component interventions. The interventions included various combinations of education, collaborations with pharmacists, quality circles, financial incentives and feedback on prescribing practices.

Five of the seven studies of multiple component interventions reported significant improvements in rates of generic prescribing associated with the intervention. However, only one of these was a randomised trial[17] and that trial was deemed to be at relatively high risk of bias. Similarly, two out of three studies with relatively similar interventions from the UK reported positive results, though one was not statistically significant.[17, 24] One study[23] differed from the others by incorporating financial incentives (which are considered possibly effective based on systematic review evidence) and by being based on a specific theory of behaviour change. A major limitation of these studies is that they were conducted between 1998 and 2002, so their relevance to the present-day NHS may be questionable. In addition, only five primary studies out of 13 were from the UK. Overall, the evidence on multiple component interventions, as with that for specific single interventions appears too weak and heterogeneous to provide clear guidance on how generic prescribing might be further improved.

Strengths and limitations of the review process

We searched several different databases for published as well as unpublished studies. The study quality was assessed systematically and taken into consideration in the synthesis. Appropriate methods were employed to minimise reviewer bias and error in all stages of the review process. We included only English-language studies for the rapid review, both for practical reasons related to the resources available, and because we were primarily interested in studies which are relevant to the UK NHS setting. While this might have led to the risk of relevant studies being overlooked, in practice the risk is likely to be small.

A feature of this project was the adoption of a two-stage approach, with an initial mapping of synthesised evidence followed by a review of primary studies guided by the results of the first stage. Examination of the available systematic reviews of interventions to improve prescribing allowed us to identify financial incentives as an intervention with a reasonable evidence base of research relevant to the UK NHS. This in turn reduced the work involved in the review of primary literature.

Our main focus was on the effectiveness of interventions regardless of setting but we recognise that the context for generic prescribing differs widely between health systems. In particular, low and middle income countries (LMICs) have very different issues to developed countries like the UK. Given the limited evidence found, we did not exclude studies conducted in LMICs from the synthesis. However, only one systematic review and two primary studies came into this category and excluding studies from LMICs is unlikely to have affected our conclusions.

Limitations of the evidence base

Even though most interventions had positive results various methodological weaknesses especially in randomisation and allocation concealment may have biased their findings. Only two of the primary studies included in our rapid review were RCTs.[17] In addition most of the studies had small sample sizes. Most of the studies attracted participants who had expressed an interest in generic prescribing or who were already involved in fundholding; therefore, they have had increased motivation to save money by prescribing generic drugs which could overestimate the effects. In addition, the long term effects on generic prescribing were not reported, so it was unclear whether the observed effects were sustainable in the longer run. However, it is arguable that studies reporting benefit up to 12 months suggest that the effects can be sustained.

Implications for policy and practice

Generic prescribing in the UK NHS is already at a high level and achievement of 100% generic prescribing is neither feasible nor desirable. It is well established that thoughtless implementation of policy initiatives to replace branded drugs by generic equivalents may result in confusion for patients or in some cases actual harm.[30, 31] Indeed, the Better Care, Better Value (BCBV) indicators, introduced to support prescribing of generic proton pump inhibitors, statins and ACE inhibitors are apparently no longer published, possibly reflecting concerns that they may have been used inappropriately to set targets for financial savings.[32] However, variations between areas suggest that further improvement is still possible.

A paper published too late for consideration for inclusion in our review outlines measures in the UK (Scotland) to encourage prescribing of generic drugs using the INN (international non-proprietary name).[33] Some European countries have systems of compulsory INN prescribing,[34] but as noted above this option has been ruled out as an option by the Department of Health. A further issue in Europe with limited relevance for the UK is the availability of branded generic drugs in some countries. Interventions to promote the use of these agents are similar to those for generic drugs generally, e.g. generic substitution,[35] and educational initiatives. In some healthcare systems patients may be required to meet the additional costs themselves if they are prescribed a product more expensive than the recommended (reference priced) generic drug.[36]

The main focus in the UK has been on encouraging use of generics versus patented products within a class or related class. This assumes that the products are similar in all or nearly all patients at appropriate doses, as in the drug classes covered by the BCBV indicators. There are classes of drugs for which generic forms are available but this assumption does not hold, for example atypical antipsychotics. This is because individual antipsychotic drugs differ in their adverse effect profiles and clinicians need to select the most appropriate agent based on the patient's characteristics and preferences. A recent non-systematic review found that the availability of generic risperidone in Scotland had no appreciable effect on prescribing patterns, although the authors suggested that there was potential to increase prescribing of generic atypical antipsychotics through educational activities.[37]

Evidence from a Cochrane systematic review suggests possible benefits of financial incentives to support generic prescribing.[6] The UK studies included in the review mainly relate to GP fundholding which is no longer used. Many areas use prescribing incentive schemes to support cost-effective prescribing.[29] Incentive schemes may focus on specific drugs or drug classes in accordance with local conditions.

The review of primary studies suggested that a range of interventions may be effective in increasing rates of generic prescribing. However, limitations in the evidence base make it difficult to identify any specific intervention or combination of interventions particularly suitable for implementation in

the contemporary NHS setting. Decision-makers will need to consider which interventions appear most suitable to their specific setting. They may also want to consider whether the likely benefits of an intervention will outweigh its costs given the high levels of generic prescribing achieved by existing measures.

A number of systematic reviews of better quality evidence have shown modest absolute increases in desired health professional behaviours associated with interventions like audit and feedback, educational meetings and outreach and reminder systems.[13, 38] Given the relative consistency of results, this evidence in conjunction with our review findings could help in estimating the likely impact of a proposed intervention on generic prescribing behaviour.

Prescribing restrictions or removal of products from reimbursement lists to encourage generic prescribing has been used in some European countries but not in the UK. An example is switching from patented to generic statins in Norway[39] and Finland.[40] A related approach is to lift restrictions for generic forms only, as was done for angiotensin receptor blockers in some European countries when generic losartan became available.[41] However, such policies are unlikely to be applied in the UK and as whole health system policy interventions they are outside the scope of this review.

Implications for research

Although high quality RCTs would improve the evidence base, it is unclear whether such studies would be justified, as the sample size required to demonstrate a benefit over current best practice would be large and the absolute improvement would be small. However, trials of specific interventions targeted at practices or individuals with particularly low levels of generic prescribing could be considered. Such trials should evaluate interventions that have proved successful in changing other types of behaviour and are based on a robust theory of behaviour change.

Given the existence of substantial variation between areas and individual general practices, further research may be helpful to explore the reasons for this. Research could focus on specific highly prescribed drugs with generic forms available (e.g. statins) and use a qualitative or mixed methods design.

Conclusions

Although several interventions look promising, complex interventions, methodological weaknesses and conflicting results limit the validity and applicability of the findings. In particular most of the available studies were conducted with baseline rates of generic prescribing significantly lower than the NHS is currently achieving. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

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CONTRIBUTORSHIP STATEMENT

MH designed the search strategy. TMB, DC and CMcD performed the literature search, screened the titles and abstracts and managed the references. All 3 reviewers (TMB, DC and CMcD) screened the retrieved papers against inclusion criteria and independently performed the data extraction and quality evaluation assessment for the review. All 3 reviewers interpreted the results. All authors have approved the manuscript and given approval for it to be published.

COMPETING INTERESTS

None

DATA SHARING STATEMENT

Extra data can be accessed by e-mailing duncan.chambers@york.ac.uk

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Title: Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review

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ABSTRACT

Objective: To summarise evidence on the effectiveness of behaviour change interventions to encourage prescribing of generic forms of prescription drugs where clinically appropriate in the UK NHS and similar settings.

Design: systematic review

Search strategy: We conducted a rapid evidence synthesis in two stages: Firstly, we searched databases such as the Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE), for systematic reviews of interventions that reported outcomes related to utilisation of generic drugs. For the second stage, we searched several databases including MEDLINE and EMBASE to identify primary studies of any interventions not adequately covered by systematic reviews.

Data extraction and quality assessment: Data were extracted into a standardised data extraction form. Standardised quality assessment tools were used to assess study quality. Two reviewers were involved in data extraction and quality assessment.

Results: Ten reviews were included for the initial evidence synthesis but most were of limited usefulness to our focused review question. One review evaluated the effect of prescribing policies using financial incentives and showed an increase in generic prescribing. Thirteen primary studies of other interventions were included for the rapid review. Two studies showed an increase in percentage of overall generic prescribing with an educational intervention; two studies showed improvement in generic prescribing rates when physicians collaborated with pharmacists, though in one study this was not statistically significant; two US studies showed improvements in generic prescribing with electronic prescribing. Five out of seven studies showed positive results with multi-faceted interventions.

Conclusions: The existing evidence remains insufficient to determine which behaviour change intervention or combination of interventions is most effective due to methodological weaknesses and conflicting results. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

Article Summary

'Strengths and limitations of this study'

- Appropriate use of generic medicines is important for healthcare systems to make optimum use of limited resources. In England, rates of prescribing by generic name are over 80% overall but there is evidence of variation between regions and individual prescribers.
- We have synthesised evidence from systematic and primary studies that have evaluated the effectiveness of interventions to promote generic prescribing at the level of the individual prescriber or GP practice.
- The study brings together evidence on a wide range of behaviour change interventions and identifies a number of potentially effective approaches.
- Limitations of the evidence base make it difficult to draw any firm conclusions about the relative effectiveness of different approaches. Recent evidence from UK NHS settings is particularly lacking.
- Given the uncertainty around the evidence base, decision-makers in settings where only small improvements in generic prescribing rates are likely to be achievable should take into account the practicality and costs of the intervention before implementing measures designed to further increase generic prescribing rates.

BACKGROUND

Generic medicines, which are the substitutes of original (branded) medicines with the same quality, safety and efficacy,–[1] offer an interesting opportunity for governments and healthcare payers to contain escalating healthcare budgets as their prices tend to be 10–80% lower than their proprietary equivalents.[2] In England the proportion of prescriptions prescribed generically (i.e. by non-proprietary name rather than brand name) increased from 76% in 2002 to 83.6% in 2012.[3]

Despite the trend of increasing generic prescribing rates there is thought to be room for greater efficiency. In 2008 approximately 5% of medicines were prescribed by their brand name in England when there was a generic alternative available.[4] A national Audit Office report in 2007 reported that prescriptions of generic statins (simvastatin and pravastatin) varied from 28% to 86% across English Primary Care Trusts.[5] More recent research has also identified marked variation in generic prescribing by GPs (for data on statin prescriptions in England, see www.prescribinganalytics.com).

In 2009, the Department of Health consulted on a proposal for the introduction of generic substitution (allowing pharmacists to fulfil a prescription for a branded medicine by dispensing a generic equivalent) in primary care in England. However, after considering the responses to the consultation, the Government decided not to progress the proposal further.[4] As an alternative it was suggested that 'other, less nationally prescriptive mechanisms for further supporting the use of generic medicines can be explored'.

We have undertaken a rapid evidence synthesis to inform decision-makers about the evidence base for interventions that might be applied to increase generic prescribing at the level of the individual or small units such as general practices.

Aims/objectives

To identify and summarise relevant research evidence using existing synthesised evidence sources (systematic reviews) supplemented as necessary by a rapid systematic review of primary research. The project aims to benefit the UK NHS by increasing the accessibility of the relevant evidence and by identifying gaps that need to be filled by further research.

Methods

We conducted this rapid evidence synthesis in two stages: an initial mapping of existing sources of synthesised evidence followed by rapid systematic review of the primary research literature, for interventions not covered by previous reviews. We registered the protocol of this review on PROSPERO the international prospective register of systematic reviews (registration number CRD42013004443).

Mapping of synthesised evidence

We searched the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment (HTA) database and Health Systems Evidence for the systematic reviews to map the existing sources of synthesised evidence. Terms relating to prescribing were combined using the Boolean operator AND with terms for generic drugs. No date or language limits were applied.

Systematic reviews, HTA reports and overviews were included if they evaluated the effectiveness or efficacy of an intervention and reported an outcome or outcomes related to utilisation (prescribing or dispensing) of generic drugs regardless of indication, setting or type of healthcare system. One reviewer examined the search results to identify potentially relevant reports. Full texts of potentially relevant reports were assessed for inclusion by two reviewers independently. Any disagreements were resolved by discussion and if necessary by involving a third reviewer.

Essential details of included reports were extracted using a simple data extraction form. These included the stated objectives, inclusion criteria, period covered by the search, interventions in included studies, main results and authors' conclusions. Data were extracted by one reviewer and checked by a second. The results were synthesised narratively and used to guide searching of the primary literature. In particular, interventions considered to be adequately covered by existing synthesised evidence were excluded from the rapid review of primary literature.

Rapid review of primary literature

Selection of studies

For the second stage, the previous search strategy described above was adapted for use in databases containing primary studies. We searched PubMed, MEDLINE, MEDLINE In-Process, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index of Nursing and Allied Health (CINAHL), EMBASE, Health Management Information Consortium (HMIC) and PsycINFO for studies published in English language during the period between 1985 and May 2013 (see supplementary).

Primary studies evaluating interventions designed to promote prescribing and/or dispensing of generic drugs were included. The main focus was interventions applied to individuals but interventions at the group (e.g. general practice) level were also eligible. Studies which looked at

financial incentives as a main intervention were excluded as there were already reviews covering those aspects in generic prescribing. We excluded interventions considered not applicable in UK NHS settings and also generic substitution because the Department of Health decided after a consultation exercise not to introduce such a policy. Randomised or quasi-randomised controlled trials, controlled before-and-after (CBA) studies and interrupted time-series (ITS), based on Cochrane EPOC (Effective Practice and Organisation of Care) Group definitions, were eligible. The primary outcome was any measure of rate of prescribing or dispensing of generic drugs (relative to comparator group or change over time). Studies of barriers and facilitators of generic prescribing were also included but this will be reported elsewhere (a full report is available from the authors).

Records were initially screened by one reviewer to remove obviously irrelevant material, the remaining records and full papers were screened independently by two reviewers. Any disagreements were discussed with a third reviewer.

Data extraction and quality assessment

Data on objectives, setting, study design, participants, details of the intervention(s) and results/conclusions related to rates of generic prescribing/dispensing were extracted. Risk of bias was assessed using the criteria of the Cochrane EPOC Group. This was undertaken by one reviewer and checked by a second; disagreements were resolved by discussion.

Methods of synthesis

The substantial heterogeneity of interventions and method across studies precluded meta-analysis and we therefore reported in a narrative synthesis. Studies were grouped by type of intervention or interventions.

Results

Mapping of synthesised evidence

The search identified 356 potentially relevant references: 40 full papers were ordered; 10 systematic reviews (9 reviews and one overview of reviews) which evaluated interventions such as financial incentives, prescribing policies, cost sharing, use of computers/IT, educational interventions, audit and feedback (Table 1).

Most of the reviews had broad objectives and did not focus specifically on interventions targeted at increasing rates of generic prescribing, for example they looked at prescribing behaviour in general rather than specifically generic prescribing. As a result there was often limited synthesis and discussion of the outcomes related to generic prescribing. This made it difficult to interpret the extent of the impact of the intervention on generic drug use in some studies.

Only two reviews had a reasonable volume of primary studies reporting generic prescribing outcomes.[6, 7] The most informative review for our research question and the UK specific focus was a Cochrane review evaluating the effect of prescribing policies using financial incentives. [6] There was evidence across all the studies included in the review of an increase in generic prescribing with fundholding, though this was not statistically significant in all the studies. In the controlled before and after studies the increase ranged from 8.8% to 13.4% at 12 months and between 4% and 17.2% at 24 months. In one controlled interrupted time series there was a 15% increase in generic prescribing (range -43.7% to 190.5%) at 12 months; in a second study using the same design there was an 18.3% increase (range 13.6% to 23%). The authors reported that budgeting funds to a group of or individual physicians (i.e. giving them financial responsibility for their own budget) increased

the use of generic drugs. [6] However, the majority of studies had serious limitations and the authors cautioned that the results should be interpreted with care.[6]

The second review with a strong focus on generic prescribing, which was less relevant to the UK NHS, focused on policy intervention in low and middle income countries. The review found insufficient evidence to determine which pro-generic policies increase utilisation of generic medicines in this setting.[7] The remainder of the reviews were more specific to the US healthcare system and less relevant to the UK NHS. In addition, six of the reviews contained only a single primary study reporting generic prescribing outcomes.[8-13] Overall, most of the interventions considered in the reviews showed an increase in generic prescribing.

Table 1: Included systematic reviews

Study details	Literature search end date	Summary of authors' objective	Intervention
Carroll (2003)[8]	09/2002	To evaluate whether community pharmacists have the ability to influence prescribing decisions and the extent to which they do so	Pharmacist interventions
Figueiras (2001)[11]	1997	To propose effective continuing medical education strategies to improve prescribing practices	Educational strategies
Gibson (2005)[14]	04/2005	To determine whether patients respond to increased cost sharing by substituting less expensive alternatives for medications with higher levels of copayments or coinsurance	Cost-sharing
Green (2010)[12]	01/2009	To determine the effects of a pharmaceutical policy restricting the reimbursement of selected medications on drug use, health care utilization, health outcomes and costs	Policy restrictions on reimbursed drugs
Ivers (2012)[13]	09/2011	To investigate the effectiveness of audit and feedback to improve processes and outcomes of care and to examine factors that could influence intervention effectiveness	Audit and feedback
Kaplan (2012)[7]	01/2012	To inquire into the nature, extent and strength of the evidence for successful implementation of pro-generic medicines policies in low and middle income countries.	Pro-generic medicines policies
Mitchell (2001)[10]	1997	To appraise findings from studies examining the impact of computers on primary care consultations	Computer systems for use by doctors during consultations
McKibbon (2011)[9]	09/2009	To review the evidence on the impact of health information technology (IT) on all phases of the medication management process	IT used in the medication management process

Sturm (2007)[6]	08/2005	To determine the effects of prescribing policies using financial incentives for prescribers on drug use, healthcare utilisation, health outcomes and costs	Financial incentives (fundholding, drug budgets)

Rapid review of primary studies

A total of 11,690 records were identified from the searches of which 6144 records were potentially relevant for the rapid review (Figure 1). On the basis of screening title and abstracts, 99 full papers were ordered for further assessment. In addition, one paper was retrieved from hand searching, making a total of 100 full papers. Of the 100 full papers, 87 were excluded because; they did not meet the inclusion criteria, did not focus on generic prescribing or were irrelevant to the NHS. We also excluded studies of financial incentives as the main intervention as this had been adequately covered in a previous systematic review.[6] One study was unobtainable.[15]

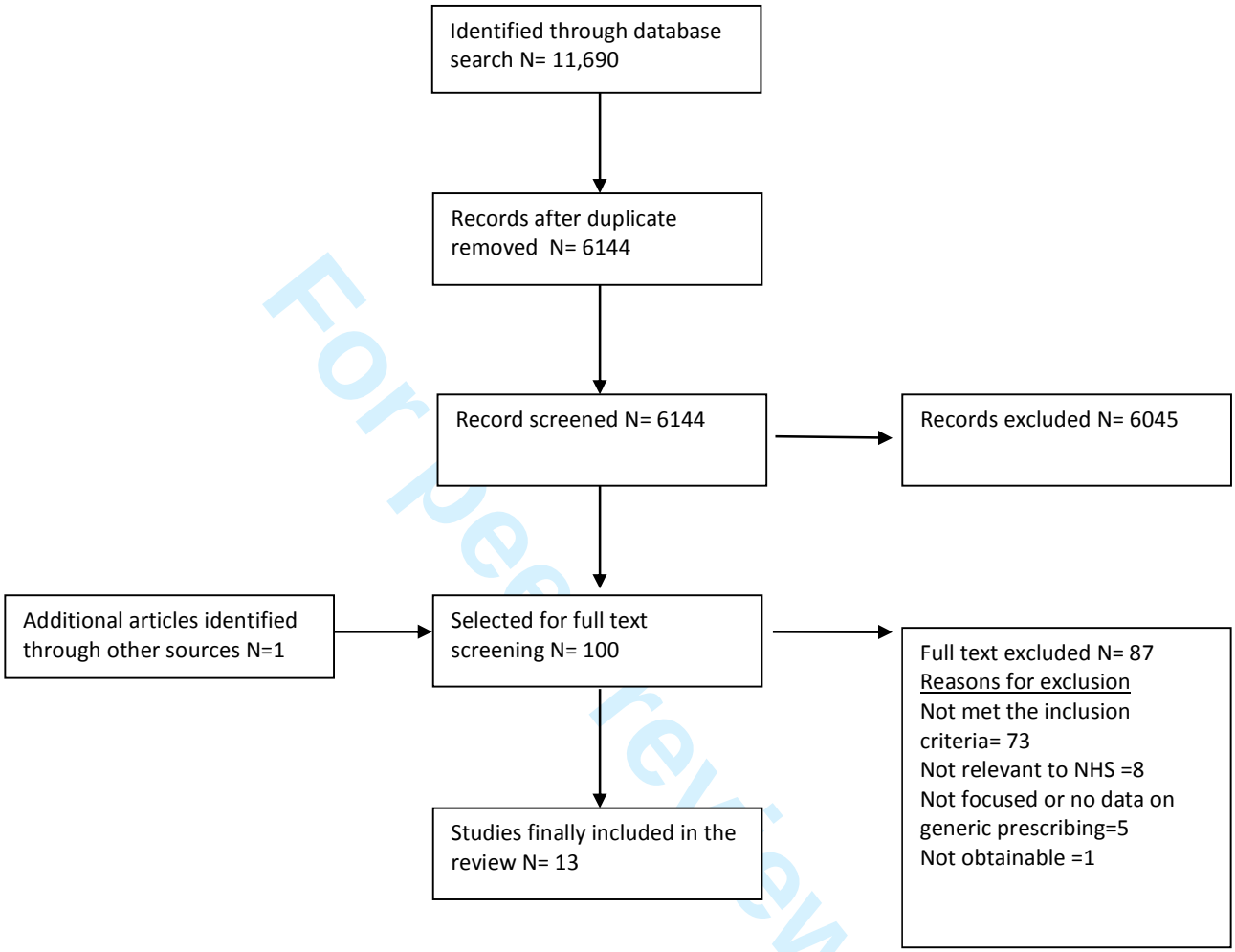

Figure 1: Study Flow Diagram

Intervention studies

Thirteen studies met the inclusion criteria: two RCTs (one individual and one cluster randomisation);[16, 17] nine CBA;[18-26] and two ITS (one with control group).[27, 28]

Most of the studies were in a primary care setting; five were conducted in the UK.[17, 21-24] The interventions were single or multi-component, and included professional educational interventions (2 studies), physicians' collaboration with pharmacists (2 studies), electronic prescribing (2 studies), and multi-faceted interventions which also included the above interventions as well as networking, feedback and financial incentives (7 studies). Most of the control groups used usual practice or no intervention. Where reported baseline generic prescribing rates ranged from 3.12% to 69.4% in the intervention groups and 16.2% to 82% in the control groups.

Risk of bias in included intervention studies

The risk of bias results are summarised in tables 2 and 3.

Table 2: Risk of bias for RCTs and CBA studies

	1	2	3	4	5	6	7	8	9
RCTs									
Braybrook (2000)[17]	UC	H	L	H	UC	UC	L	L	-
Meyer (2001)[16]	L	L	L	UC	UC	UC	L	L	H
CBA									
Fischer (2008)[20]	H	H	L	H	H	L	L	L	L
Geoghegan (1998)[21]	H	H	L	UC	UC	L	L	L	UC
Leach (1999)[22]	H	H	L	UC	UC	L	L	L	L
Mastura (2008)[19]	H	H	H	UC	UC	H	L	L	H
Niquille (2010)[26]	H	H	UC	UC.	UC	H	L	H	-
Onion (1998)[23]	H	H	L	UC	L	L	L	L	L
Walker (2002)[24]	H	H	H	H	UC	UC	L	L	-
Wensing (2004)[25]	H	H	L	UC	L	L	L	L	H
Wensing (2009)[18]	H	H	L	UC	L	L	L	L	-

Key: 1. Sequence generation; 2. Allocation concealment; 3. Baseline measurements; 4. Baseline characteristics; 5. incomplete outcome data; 6. Blinded assessment of primary outcome; 7. Protection against contamination; 8. Selective outcome reporting; 9. Other risk of bias
H=high, L=low, UC=unclear

Table 3: Risk of bias for ITS studies

	1	2	3	4	5	6	7
Lopez-Picazo Ferrer (2002)[28]	UC	L	L	L	UC	L	H
Stenner (2010) [27]	L	L	L	L	UC	L	-

Key: 1. Intervention independent of other changes; 2. Shape of intervention effect; 3. Intervention unlikely to affect data collection; 4. Knowledge of allocated intervention adequately prevented; 5. Incomplete outcome data; 6. Selective outcome reporting; 7. Other risk of bias.
H=high, L=low, UC=unclear

Table 4: Characteristics of intervention studies

Study details Country/setting	Populations	Intervention	Control
Cluster RCT			
Braybrook (2000)[17] UK/ Primary care	General medical practices contracted to Gwent Health Authority (September 1993 to March 2004)	Active feedback (N= 34 practices): Visits from pharmaceutical prescribing adviser to present prescribing analysis and cost (PACT) data concerning NSAID use and to promote prescribing review.	Passive feedback (N=32 practices): Practice specific prescribing analysis workbook containing similar information to the intervention. Reference group (N=22 practices): Received no information on NSAIDs from the prescribing adviser
RCT			
Meyer (2001) [16] South Africa/ Primary health care clinics	Primary health care nurses in the Northern Province of South Africa (1997)	4-day effective prescribing training workshops provided by 24 provincial trainers who had previously received a generic training-of-trainers course and one week effective prescribing course. The effective prescribing training used the WHO annual Guide to Good Prescribing as a framework and problem-based learning methods were used. N=12 primary health care clinics randomised (11 analysed)	No training N=12 primary health care clinics randomised (11 analysed)
CBA			

Fischer (2008)[20] USA/ Community-based practices	Clinicians from community-based practices from Massachusetts (2003- 2005)	E-prescription with FDS (formulary decision support); E-prescription system (Pocket Script) identifies preferred medications, often generic medications N=1198 clinicians (clinicians needed to write at least 1e-priscriptions)	Unenrolled prescribers (Clinicians who did not use e-prescription) N= 34453 clinicians
Geoghegan (1998)[21] UK/ Primary care	General practices(GP) in St Helens and Knowsley	Prescribing meetings (at least six meeting a year) held between local GPs and community pharmacists, with agenda determined by GPs and pharmacists N=8 practices	Practices not participating in meetings N=50 practices
Leach (1999)[22] UK/ Primary care	Pharmacists and GP (general practitioners) practices in Dudley health authority	Prescribing advice to local GP from community pharmacists who had received relevant additional training (each practice received 4 visits a year from their community pharmacist) N= 5 practices (11 partners)	All remaining GP practices from the same health authority N=58 practices (151 partners)
Mastura (2008)[19] Malaysia/ Health clinic	Medical officers from government health clinics in Negeri Sembilan (2004)	Group academic detailing N=5 medical officers (1 clinic, 1848 prescriptions)	No intervention N=4 medical officers (1 clinic, 1525 prescriptions)
Niquille (2010)[26] Switzerland/ Primary care	General practices in the Swiss Canton of Fribourg who were non-dispensing physicians (1999-2007)	Quality circles (N=6 circles; 6 pharmacists and 24 GPs) Groups were moderated by specifically trained pharmacists (intervention included networking, feedback, interdisciplinary continuing education).	No intervention (N= 79 to 753 GPs each year since 1999)

Onion (1998)[23] UK/ Primary care	General practitioners (GP) in Wirral Health Authority (1992-1993)	N=10 practices Based on Ford's motivational systems theory. Included financial incentive; standard setting for improvement; interactive education; agreed performance standards for cost savings and clinical audit	No intervention (N=10 practices)
Walker (2002)[24] UK/ Primary care	General Practitioners involved in a commissioning group pilot in Southern Derbyshire (1997 – 1999)	N=9 practices; 36 GPs Pharmaceutical adviser 1 day a week for a year. Intervention included practice comparison feedback, peer review meetings, and prescribing recommendations.	No intervention (N=9 practices; 44 GPs)
Wensing (2004)[25] Germany/ Primary care	Primary care doctors from the Sachsen-Anhalt region, mainly from single-handed practices (1996-1998)	Quality circles (N=10 circles; 90 GPs) Groups were moderated by specifically trained primary care physicians. Intervention included educational session and structured feedback on individual prescribing practices.	No intervention (N=87 GPs): Random sample of physicians in the same region
Wensing (2009)[18] Germany/ Primary care	Primary care physicians (GPs) from 3 regions (2001-2003)	Quality circles (N=152 circles; 1090 GPs) Nine meetings. Intervention included provision of evidence based information and repeated feedback on individual prescribing patterns).	No intervention (N=2090 GPs): Random sample of physicians in the same region
ITS			
Lopez-Picazo (2002)[28]	Primary care teams from four of the six health areas of	N=45 practices; 339 GPs Each individual received information about individual, team and health district prescribing	N/A

Spain/ Primary care	Murcia (1998-2000)	behaviour; regularly updated information on generic drugs; up to three clinical outreach sessions with each primary care team; and specific generic prescribing goals and financial incentives to achieve the goals.	
Stenner (2010)27 USA/ Vanderbilt Medical Group's outpatient clinics	Health care practitioners at a single medical centre, Vanderbilt University Medical Centre (VUMC) (2005-2008)	E prescribing system(Rx-Star) Changes were made to how medications were displayed on the current e-prescribing system; available generic formulations were displayed in a larger bolder font and were listed above brand name medications regardless of whether the practitioner searched for generic or brand name N=1.1 million electronic prescriptions from 2000 unique prescribers	Hand-written prescriptions that were filled at a single VUMC outpatient pharmacy (without e-prescribing, non Rx-Star) N=4456 randomly sampled prescriptions

NA=Not applicable

Narrative synthesis of intervention studies

Educational interventions

One CBA [19] and one RCT[16], both had methodological limitations, evaluated an educational interventions. There was a statistically significant increase in use of generic drugs for upper respiratory tract infection at three months follow-up in the RCT (p<0.05). [16] However, the authors reported that only 30 prescriptions per clinic were analysed retrospectively and it was unclear how they selected prescriptions for analysis. [16] In the CBA study, the proportion of prescriptions using the brand name reduced in the intervention group compared to control but there was a very strong imbalance at baseline (Intervention: Pre 33.9%, Post 19%; Control: Pre 82%; post 88.1%).[19] Overall, these studies suggest that educational interventions may be able to increase generic prescribing rates but limitations in methodology and differences in setting, as well as the small number of studies, limit the conclusions that can be drawn from them.

Physicians' collaboration with pharmacists

Two CBA studies evaluated the effectiveness of pharmacists working with General Practitioners (GPs).[21, 22] There was some baseline imbalance in one study.[22] Both studies showed improvement in generic prescribing rates, though in one study this was not statistically significant (p=0.338)[21]. In the second study there was a mean increase over baseline in total generic prescribing in the intervention group compared with control: 9/1000 at 3 months (P > 0.05), 10/1000 at 6 months (P > 0.05), 35/1000 at 12 months (P <0.01).[22] The differing results of these two studies together with their relatively weak design provide limited evidence as to whether collaboration between physicians and pharmacists can improve generic prescribing rates.

Electronic prescribing (e-prescribing)

Two studies (one CBA and one ITS), conducted in the USA, reported the effect of an e-prescribing system which identified generic medications.[20, 27] The risk of bias was relatively low in the ITS study whereas in the CBA study there were slight baseline imbalances. Both studies reported an increase in generic prescribing with e-prescribing when compared to control. In the ITS the proportion of generic prescribing increased from baseline in the intervention group (pre 32% to post 50%) and also very slightly increased in the control group (pre 29% to post 31% of hand-written prescriptions). The proportion of generic prescribing was still higher in intervention group compared to control after two years post intervention (p<0.0001) and increased significantly in every speciality with e-prescribing (range 11.8% to 62.5%).[27]

Similarly, the CBA study reported that the e-prescription group increased their generic prescribing from baseline compared to control (absolute change 3.7% vs. 2.6%). After adjusting for baseline differences between prescribers and for changes over time e-prescription corresponded to a 3.3% increase in generic prescribing. [20]

However, the relevance of this evidence to the UK is uncertain given the differences between the US and UK health systems and the fact that e-prescribing systems are already widespread.

Multi-faceted interventions

Seven studies examined multi-component interventions;[17, 18, 23-26, 28] five CBA studies, one cluster RCT and one ITS.

In three studies (one cluster RCT and two CBA), a major component of the intervention was meetings between GPs and pharmacists who were giving regular feedback and prescribing recommendations.[17, 24, 26] All three studies had high or unclear risk of bias for most criteria. Two were conducted in the UK.[17, 24] One study reported no significant increase in the percentage of overall

generic drugs compared to control (p=0.17) [24] whereas the other two studies[17, 26] reported increases in generic prescribing in the intervention group. One CBA study reported that the intervention group was always higher than control for the five main cardiovascular classes of drugs for 3 years but the difference between the two groups reduced over time in each of the drug classes.[26] The cluster RCT study reported that active and passive feedback increased generic prescribing of (non-steroidal anti-inflammatory drugs (NSAIDs) compared to the reference group (pre and post differences in active, passive and reference group: 7%, 6%, and 4%). [17]

Two CBA studies, involving 90 and 1090 GPs from Germany, used quality circles which were moderated by primary care doctors and involved structured feedback on individual prescribing patterns and educational sessions.[18, 25] Both studies were high risk of bias in randomisation and allocation concealment and unclear risk in baseline characteristics. The 2009 study,[18] which involved 1090 GPs, reported no significant difference in prescribing generic drugs compared to control whereas the 2004 study,[25] which involved 90 GPs, reported significant increase in the percentage of generic prescribing in the intervention group (OR 1.10, 95%CI 1.08 to 1.13).

One CBA study which involved GPs from 10 practices from the UK used multiple interventions which included financial incentives, setting of standards for improvement, interactive education, agreed performance for cost savings and clinical audit.[23] The risk of bias was high for randomisation and allocation concealment, and unclear for baseline characteristics. The authors reported that the proportion of generic prescribing increased in the intervention group by 5% compared with the control (OR 1.22, 95% CI 1.18 to 1.28, p<0.0001). However, differences in the two groups started to decline after a further three months. [23]

Finally we included an ITS study which involved 339 family physicians from 45 primary care teams from Spain who received personalised information regarding prescribing behaviour, updated information cards on generic drugs and a letter, clinical outreach session with each primary care team, specific prescribing goal and financial incentives.[28] The risk of bias was low for most criteria, however it was unclear whether the interventions were independent of other changes. The study reported increased generic prescribing in the intervention group. The mean percentage of generic prescriptions for the 3 month period immediately before the intervention was 2.79% and for the 3 months immediately following the end of the intervention was 17.63%; absolute improvement was 14.84% and relative improvement was 15.27%.[28]

Discussion

Summary of main results

Our objective was to identify and summarise the research evidence on interventions aimed at improving generic prescribing rates. We took a two stage approach: first we identified and summarised existing synthesised evidence. Second, as little synthesised evidence is available, we conducted a rapid review of the primary literature on interventions to improve rates of generic prescribing.

Only two systematic reviews focused specifically on generic prescribing behaviours. The evidence from a Cochrane review suggests possible benefits of financial incentives to support generic prescribing.[6] Many areas currently use prescribing incentive schemes to support cost-effective prescribing and this strategy is endorsed, subject to suitable safeguards, by the English Department

of Health.[29] The second review with a strong focus on generic prescribing, which was less relevant to the NHS, focused on policy intervention in low and middle income countries.

We identified thirteen primary studies which evaluated the effects of an intervention to improve generic drug utilisation. Two studies evaluated an educational intervention and showed an increase in the percentage of overall prescribing of generic drugs; two studies which evaluated the effect of physicians collaborating with pharmacists showed improvement in generic prescribing rates, though in one study this was not statistically significant; and two studies from the USA which evaluated e-electronic prescribing showed improvements in generic prescribing. Seven studies used multi-component interventions. The interventions included various combinations of education, collaborations with pharmacists, quality circles, financial incentives and feedback on prescribing practices.

Five of the seven studies of multiple component interventions reported significant improvements in rates of generic prescribing associated with the intervention. However, only one of these was a randomised trial[17] and that trial was deemed to be at relatively high risk of bias. Similarly, two out of three studies with relatively similar interventions from the UK reported positive results, though one was not statistically significant.[17, 24] One study[23] differed from the others by incorporating financial incentives (which are considered possibly effective based on systematic review evidence) and by being based on a specific theory of behaviour change. A major limitation of these studies is that they were conducted between 1998 and 2002, so their relevance to the present-day NHS may be questionable. In addition, only five primary studies out of 13 were from the UK. Overall, the evidence on multiple component interventions, as with that for specific single interventions appears too weak and heterogeneous to provide clear guidance on how generic prescribing might be further improved.

Strengths and limitations of the review process

We searched several different databases for published as well as unpublished studies. The study quality was assessed systematically and taken into consideration in the synthesis. Appropriate methods were employed to minimise reviewer bias and error in all stages of the review process. We included only English-language studies for the rapid review, both for practical reasons related to the resources available, and because we were primarily interested in studies which are relevant to the UK NHS setting. While this might have led to the risk of relevant studies being overlooked, in practice the risk is likely to be small.

A feature of this project was the adoption of a two-stage approach, with an initial mapping of synthesised evidence followed by a review of primary studies guided by the results of the first stage. Examination of the available systematic reviews of interventions to improve prescribing allowed us to identify financial incentives as an intervention with a reasonable evidence base of research relevant to the UK NHS. This in turn reduced the work involved in the review of primary literature.

Our main focus was on the effectiveness of interventions regardless of setting but we recognise that the context for generic prescribing differs widely between health systems. In particular, low and middle income countries (LMICs) have very different issues to developed countries like the UK. Given the limited evidence found, we did not exclude studies conducted in LMICs from the synthesis. However, only one systematic review and two primary studies came into this category and excluding studies from LMICs is unlikely to have affected our conclusions.

Limitations of the evidence base

Even though most interventions had positive results various methodological weaknesses especially in randomisation and allocation concealment may have biased their findings. Only two of the primary studies included in our rapid review were RCTs.[17] In addition most of the studies had small sample sizes. Most of the studies attracted participants who had expressed an interest in generic prescribing or who were already involved in fundholding; therefore, they have had increased motivation to save money by prescribing generic drugs which could overestimate the effects. In addition, the long term effects on generic prescribing were not reported, so it was unclear whether the observed effects were sustainable in the longer run. However, it is arguable that studies reporting benefit up to 12 months suggest that the effects can be sustained.

Implications for policy and practice

Generic prescribing in the UK NHS is already at a high level and achievement of 100% generic prescribing is neither feasible nor desirable. It is well established that thoughtless implementation of policy initiatives to replace branded drugs by generic equivalents may result in confusion for patients or in some cases actual harm.{Duerden, 2010 #984;Ferner, 2010 #1024} Indeed, the Better Care, Better Value (BCBV) indicators, introduced to support prescribing of generic proton pump inhibitors, statins and ACE inhibitors are apparently no longer published, possibly reflecting concerns that they may have been used inappropriately to set targets for financial savings.{Department of Health, 2011 #11744} However, variations between areas suggest that further improvement is still possible.

A paper published too late for consideration for inclusion in our review outlines measures in the UK (Scotland) to encourage prescribing of generic drugs using the INN (international non-proprietary name).{Godman, 2013 #11746} Some European countries have systems of compulsory INN prescribing,{Garuoliene, 2011 #3591} but as noted above this option has been ruled out as an option by the Department of Health. A further issue in Europe with limited relevance for the UK is the availability of branded generic drugs in some countries. Interventions to promote the use of these agents are similar to those for generic drugs generally, e.g. generic substitution,{Andersson, 2008 #1440} and educational initiatives. In some healthcare systems patients may be required to meet the additional costs themselves if they are prescribed a product more expensive than the recommended (reference priced) generic drug.{Dylst, 2011 #611}

The main focus in the UK has been on encouraging use of generics versus patented products within a class or related class. This assumes that the products are similar in all or nearly all patients at appropriate doses, as in the drug classes covered by the BCBV indicators. There are classes of drugs for which generic forms are available but this assumption does not hold, for example atypical antipsychotics. This is because individual antipsychotic drugs differ in their adverse effect profiles and clinicians need to select the most appropriate agent based on the patient's characteristics and preferences. A recent non-systematic review found that the availability of generic risperidone in Scotland had no appreciable effect on prescribing patterns, although the authors suggested that there was potential to increase prescribing of generic atypical antipsychotics through educational activities.{Bennie, 2013 #62}

Evidence from a Cochrane systematic review suggests possible benefits of financial incentives to support generic prescribing.[6] The UK studies included in the review mainly relate to GP fundholding which is no longer used. Many areas use prescribing incentive schemes to support cost-effective prescribing.[29] Incentive schemes may focus on specific drugs or drug classes in accordance with local conditions.

The review of primary studies suggested that a range of interventions may be effective in increasing rates of generic prescribing. However, limitations in the evidence base make it difficult to identify

any specific intervention or combination of interventions particularly suitable for implementation in the contemporary NHS setting. Decision-makers will need to consider which interventions appear most suitable to their specific setting. They may also want to consider whether the likely benefits of an intervention will outweigh its costs given the high levels of generic prescribing achieved by existing measures.

A number of systematic reviews of better quality evidence have shown modest absolute increases in desired health professional behaviours associated with interventions like audit and feedback, educational meetings and outreach and reminder systems.[13, 30] Given the relative consistency of results, this evidence in conjunction with our review findings could help in estimating the likely impact of a proposed intervention on generic prescribing behaviour.

Prescribing restrictions or removal of products from reimbursement lists to encourage generic prescribing has been used in some European countries but not in the UK. An example is switching from patented to generic statins in Norway{Sakshaug, 2007 #11728} and Finland.{Martikainen, 2010 #11745} A related approach is to lift restrictions for generic forms only, as was done for angiotensin receptor blockers in some European countries when generic losartan became available.{Bucsics, 2012 #68} However, such policies are unlikely to be applied in the UK and as whole health system policy interventions they are outside the scope of this review.

Implications for research

Although high quality RCTs would improve the evidence base, it is unclear whether such studies would be justified, as the sample size required to demonstrate a benefit over current best practice would be large and the absolute improvement would be small. However, trials of specific interventions targeted at practices or individuals with particularly low levels of generic prescribing could be considered. Such trials should evaluate interventions that have proved successful in changing other types of behaviour and are based on a robust theory of behaviour change.

Given the existence of substantial variation between areas and individual general practices, further research may be helpful to explore the reasons for this. Research could focus on specific highly prescribed drugs with generic forms available (e.g. statins) and use a qualitative or mixed methods design.

Conclusions

Although several interventions look promising, complex interventions, methodological weaknesses and conflicting results limit the validity and applicability of the findings. In particular most of the available studies were conducted with baseline rates of generic prescribing significantly lower than the NHS is currently achieving. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

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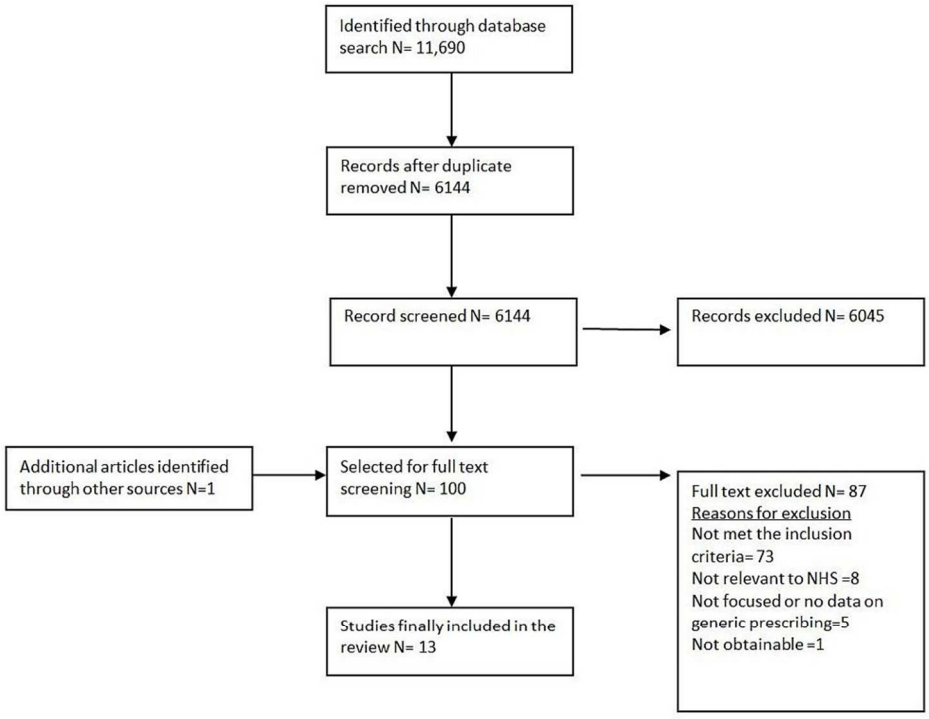

90x66mm (300 x 300 DPI)

SUPPLEMENTARY

Search strategies for the rapid review of primary literature

Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Library, Wiley

http://onlinelibrary.wiley.com/

Issue 4 of 12, April 2013

Search date: 17th May 2103

Records retrieved: 188

ID	Search	Hits
#1	MeSH descriptor: [Physician's Practice Patterns] this term only	945
#2	MeSH descriptor: [Prescriptions] this term only	70
#3	MeSH descriptor: [Drug Prescriptions] this term only	417
#4	MeSH descriptor: [Electronic Prescribing] this term only	18
#5	MeSH descriptor: [Medical Order Entry Systems] this term only	49
#6	MeSH descriptor: [Medication Systems] this term only	24
#7	MeSH descriptor: [Medication Systems, Hospital] this term only	41
#8	(prescrib* or eprescrib*):ti,ab,kw	6610
#9	(prescription* or eprescription*):ti,ab,kw	3508
#10	dispens*:ti,ab,kw	788
#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	10382
#12	MeSH descriptor: [Drugs, Generic] this term only	199
#13	generic*:ti,ab,kw	1345
#14	(non next proprietary):ti,ab,kw	7
#15	#12 or #13 or #14	1352
#16	#11 and #15	109
#17	MeSH descriptor: [Drug Substitution] this term only	58
#18	(substitut* near/2 (generic* or (non next proprietary) or therapeutic*)):ti,ab,kw	74
#19	#17 or #18	131
#20	#16 or #19 from 1985 to 2013, in Trials	188

Key:

MeSH descriptor = indexing term (MeSH heading)

* = truncation

:ti,ab,kw = terms in either title or abstract or keyword fields

near/2 = terms within two word of each other (any order)

next = terms are next to each other

CINAHL via Ebsco

http://www.ebsco.com/

Inception – 10th May 2013

Search date: 17th May 2013

Records retrieved: 562

#	Query	Results
S24	S16 OR S22 Limiters - English Language; Published Date from: 19850101-20131231	562
S23	S16 OR S22	571
S22	S17 OR S18 OR S19 OR S20 OR S21	115
S21	TI substitut* N2 therapeutic* OR AB substitut* N2 therapeutic*	26
S20	TI substitut* N2 "non proprietary" OR AB substitut* N2 "non proprietary"	0
S19	TI substitut* N2 nonproprietary OR AB substitut* N2 nonproprietary	0
S18	TI substitut* N2 non-proprietary OR AB substitut* N2 non-proprietary	0
S17	TI substitut* N2 generic* OR AB substitut* N2 generic*	92
S16	S10 AND S15	506

S15	S11 OR S12 OR S13 OR S14	5,404
S14	TI "non proprietary" OR AB "non proprietary" OR TI non-proprietary OR AB non-proprietary	15
S13	TI nonproprietary OR AB nonproprietary	48
S12	TI generic* OR AB generic*	4,528
S11	(MH "Drugs, Generic")	1,568
S10	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9	38,541
S9	TI dispens* OR AB dispens*	2,059
S8	TI prescription* OR AB prescription* OR TI eprescription* OR AB eprescription*	12,270
S7	TI prescrib* OR AB prescrib* OR TI eprescrib* OR AB eprescrib*	18,772
S6	(MH "Practice Patterns")	3,932
S5	(MH "Medication Systems")	1,052
S4	(MH "Electronic Order Entry")	1,388
S3	(MH "Prescriptions, Drug")	3,752
S2	(MH "Prescriptive Authority")	3,771
S1	(MH "Prescribing Patterns")	1,488

Key:

MH = indexing term (CINAHL heading)

* = truncation

TI = words in the title

AB = words in the abstract

" " = phrase search

N2 = terms within two words of each other (any order)

EMBASE via OvidSP

http://ovidsp.ovid.com/

1980 to 2013 week 19

Searched on: 17th May 2013

Records retrieved: 4795

1 clinical practice/ (150206)

2 prescription/ (98358)

3 electronic prescribing/ (800)

4 computerized provider order entry/ (530)

5 (prescrib$ or eprescrib$).ti,ab. (114426)

6 (prescription$ or eprescription$).ti,ab. (75360)

7 dispens$.ti,ab. (29987)

8 or/1-7 (368968)

9 generic drug/ (7959)

10 generic$.ti,ab. (31529)

11 non-proprietary.ti,ab. (171)

12 nonproprietary.ti,ab. (234)

13 or/9-12 (35545)

14 8 and 13 (4900)

15 *drug substitution/ (335)

16 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (1055)

17 15 or 16 (1316)

18 14 or 17 (5722)

19 animal/ (1816382)

20 exp animal experiment/ (1584117)

21 Nonhuman/ (4050841)

22 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh. (4570661)

23 19 or 20 or 21 or 22 (6577334)

24 exp human/ (14329978)

25 human experiment/ (311984)

26 24 or 25 (14331371)

27 23 not (23 and 26) (5088908)

28 18 not 27 (5632)

29 limit 28 to yr="1985 -Current" (5494)

30 limit 29 to english language (4795)

Key:

/ = indexing term (EMTREE heading)

exp = exploded EMTREE heading

* = focussed EMTREE heading

$ = truncation

.ti,ab. = terms in either title or abstract fields

sh = terms in the subject heading field

adj2 = terms within two words of each other (any order)

Health Management Information Consortium via OvidSP

http://ovidsp.ovid.com/

1979 to March 2013

Searched on: 17th May 2013

Records retrieved: 228

1 exp prescribing/ (3145)

2 exp prescribing costs/ (143)

3 exp prescriptions/ (631)

4 prescription charges/ or prescription drugs/ or prescription pricing authority/ (688)

5 exp drug dispensing/ (407)

6 exp medication systems/ (37)

7 (prescrib$ or eprescrib$).ti,ab. (4632)

8 (prescription$ or eprescription$).ti,ab. (2856)

9 dispens$.ti,ab. (921)

10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (8446)

11 generic drugs/ (99)

12 generic$.ti,ab. (1263)

13 non-proprietary.ti,ab. (1)

14 nonproprietary.ti,ab. (10)

15 11 or 12 or 13 or 14 (1287)

16 10 and 15 (223)

17 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (34)

18 16 or 17 (232)

19 limit 18 to yr="1985 -Current" (228)

20 limit 19 to english (228)

Key:

/ = indexing term

exp = exploded indexing term

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

MEDLINE In-Process & Other Non-Indexed Citations and MEDLINE via OvidSP
http://ovidsp.ovid.com/

1946 to 16th May 2013

Searched on: 17th May 2013

Records retrieved: 2700

1 Physician's Practice Patterns/ (38329)

2 Prescriptions/ (1760)

3 Drug Prescriptions/ (21281)

4 Electronic Prescribing/ (451)

5 Medical Order Entry Systems/ (1318)

6 Medication Systems/ (722)

7 Medication Systems, Hospital/ (3103)

8 (prescrib$ or eprescrib$).ti,ab. (81556)

9 (prescription$ or eprescription$).ti,ab. (52201)

10 dispens$.ti,ab. (24461)

11 or/1-10 (180883)

12 Drugs, Generic/ (3329)

13 generic$.ti,ab. (26385)

14 non-proprietary.ti,ab. (125)

15 nonproprietary.ti,ab. (179)

16 or/12-15 (27814)

17 11 and 16 (2230)

18 Drug Substitution/ (665)

19 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (660)

20 17 or 18 or 19 (3233)

21 exp animals/ not humans/ (3847816)

22 20 not 21 (3206)

23 limit 22 to yr="1985 -Current" (3056)

24 limit 23 to english language (2700)

Key:

/ = indexing term (MeSH heading)

exp = exploded MeSH heading

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

PsycINFO via OvidSP

http://ovidsp.ovid.com/

1806 to May week 2 2013

Searched on: 17th May 2013

Records retrieved: 354

1 exp "prescribing (drugs)"/ (2629)

2 prescription drugs/ (2248)

3 (prescrib$ or eprescrib$).ti,ab. (19193)

4 (prescription$ or eprescription$).ti,ab. (12067)

5 dispens$.ti,ab. (2312)

6 1 or 2 or 3 or 4 or 5 (30538)

7 generic drugs/ (93)

8 generic$.ti,ab. (8365)

9 non-proprietary.ti,ab. (11)

10 nonproprietary.ti,ab. (20)

11 7 or 8 or 9 or 10 (8396)

12 6 and 11 (347)

13 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (84)

14 12 or 13 (384)

15 limit 14 to yr="1985 -Current" (375)

16 limit 15 to english language (354)

Key:

/ = indexing term

exp = exploded indexing term

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

PubMed

http://www.ncbi.nlm.nih.gov/pubmed

Searched on: 17th May 2013

Records retrieved: 2863

Search	Query	Items found
#56	Search #34 OR #36 OR #48 Filters: Publication date from 1985/01/01 to 2013/12/31; English Sort by: PublicationDate	2863
#53	Search #34 OR #36 OR #48 Filters: Publication date from 1985/01/01 to 2013/12/31	3222
#52	Search #34 OR #36 OR #48	3361
#48	Search (generic*[Title/Abstract]) AND substitut*[Title/Abstract]	928
#36	Search "Drug Substitution"[Mesh]	629
#34	Search #26 AND #33	2216
#33	Search #28 OR #29 OR #30	27833
#30	Search ((non-proprietary[Title/Abstract]) OR nonproprietary[Title/Abstract]) OR "non proprietary"[Title/Abstract]	296
#29	Search generic*[Title/Abstract]	26428
#28	Search "Drugs, Generic"[Mesh]	3273
#26	Search #7 OR #10 OR #13 OR #15 OR #17 OR #20 OR #22 OR #23 OR #24 OR #25	179712
#25	Search dispens*[Title/Abstract]	23786
#24	Search (prescription*[Title/Abstract]) OR eprescription*[Title/Abstract])	52177
#23	Search (prescrib*[Title/Abstract]) OR eprescrib*[Title/Abstract]	81730
#22	Search "Medication Systems, Hospital"[Mesh]	3070
#20	Search "Medication Systems"[Mesh:NoExp]	709

Search	Query	Items found
#17	Search "Medical Order Entry Systems"[Mesh]	1281
#15	Search "Electronic Prescribing"[Mesh]	431
#13	Search "Drug Prescriptions"[Mesh:NoExp]	20964
#10	Search "Prescriptions"[Mesh:NoExp]	1732
#7	Search "Physician's Practice Patterns"[Mesh]	37546

Key:

[Mesh] = exploded indexing term (MeSH heading)

[Mesh:NoExp] = indexing term (MeSH heading) not exploded

* = truncation

[Title/Abstract]) = terms in either title or abstract

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supp
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	-
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	-
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6-8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6,8,10-13
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6, 14-15
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	-
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14-15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	-
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

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Behaviour changes interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review

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Title: Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review

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ABSTRACT

Objective: To summarise evidence on the effectiveness of behaviour change interventions to encourage prescribing of generic forms of prescription drugs where clinically appropriate in the UK NHS and similar settings.

Design: systematic review

Search strategy: We conducted a rapid evidence synthesis in two stages: Firstly, we searched databases such as the Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE), for systematic reviews of interventions that reported outcomes related to utilisation of generic drugs. For the second stage, we searched several databases including MEDLINE and EMBASE to identify primary studies of any interventions not covered by systematic reviews.

Data extraction and quality assessment: Data were extracted into a standardised data extraction form. Standardised quality assessment tools were used to assess study quality. Two reviewers were involved in data extraction and quality assessment.

Results: Ten reviews were included for the initial evidence synthesis but most were of limited usefulness to our focused review question. One review evaluated the effect of prescribing policies using financial incentives and showed an increase in generic prescribing. Thirteen primary studies of other interventions were included for the rapid review. Two studies showed an increase in percentage of overall generic prescribing with an educational intervention; two studies showed improvement in generic prescribing rates when physicians collaborated with pharmacists, though in one study this was not statistically significant; two US studies showed improvements in generic prescribing with electronic prescribing. Five out of seven studies showed positive results with multi-faceted interventions.

Conclusions: The existing evidence remains insufficient to determine which behaviour change intervention or combination of interventions is most effective due to methodological weaknesses and conflicting results. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

Article Summary

'Strengths and limitations of this study'

- Appropriate use of generic medicines is important for healthcare systems to make optimum use of limited resources. In England, rates of prescribing by generic name are over 80% overall but there is evidence of variation between regions and individual prescribers.
- We have synthesised evidence from systematic and primary studies that have evaluated the effectiveness of interventions to promote generic prescribing at the level of the individual prescriber or GP practice.
- The study brings together evidence on a wide range of behaviour change interventions and identifies a number of potentially effective approaches.
- Limitations of the evidence base make it difficult to draw any firm conclusions about the relative effectiveness of different approaches. Recent evidence from UK NHS settings is particularly lacking.
- Given the uncertainty around the evidence base, decision-makers in settings where only small improvements in generic prescribing rates are likely to be achievableshould take into account the practicality and costs of the intervention before implementing measures designed to further increase generic prescribing rates.

BACKGROUND

Generic medicines, which are the substitutes of original (branded) medicines with the same quality, safety and efficacy,[1] offer an interesting opportunity for governments and healthcare payers to contain escalating healthcare budgets as their prices tend to be 10–80% lower than their proprietary equivalents.[2]In England the proportion of prescriptions prescribed generically (i.e. by non-proprietary name rather than brand name) increased from 76% in 2002 to 83.6% in 2012.[3]

Despite the trend of increasing generic prescribing rates there is thought to be room for greater efficiency.In 2008 approximately 5% of medicines were prescribed by their brand name in England when there was a generic alternative available.[4]A national Audit Office report in 2007 reported that prescriptions of generic statins (i.e., the use of multiple sourced simvastatin and pravastatin vs. patented Lipitor and Crestor) varied from 28% to 86% across English Primary Care Trusts.[5] More recent research has also identified marked variation in generic prescribing by GPs (for data on statin prescriptions in England, see www.prescribinganalytics.com).

In 2009, the Department of Health consulted on a proposal for the introduction of generic substitution (allowing pharmacists to fulfil a prescription for a branded medicine by dispensing a generic equivalent) in primary care in England. However, after considering the responses to the consultation, the Government decided not to progress the proposal further.[4] As an alternative it was suggested that 'other, less nationally prescriptive mechanisms for further supporting the use of generic medicines can be explored'.

We have undertaken a rapid evidence synthesis to inform decision-makers about the use of generics versus patented products and the evidence base for interventions that might be applied to increase generic prescribing at the level of the individual or small units such as general practices.

Aims/objectives

To identify and summarise relevant research evidence using existing synthesised evidence sources (systematic reviews) supplemented as necessary by a rapid systematic review of primary research. The project aims to benefit the UK NHS by increasing the accessibility of the relevant evidence and by identifying gaps that need to be filled by further research.

Methods

We conducted this rapid evidence synthesis in two stages: an initial mapping of existing sources of synthesised evidence followed by rapid systematic review of the primary research literature, for interventions not covered by previous reviews. We registered the protocol of this review on PROSPERO the international prospective register of systematic reviews (registration number CRD42013004443).

Mapping of synthesised evidence

We searched the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment (HTA) database and Health Systems Evidence for the systematic reviews to map the existing sources of synthesised evidence. Terms relating to prescribing were combined using the Boolean operator AND with terms for generic drugs. No date or language limits were applied.

Systematic reviews, HTA reports and overviews were included if they evaluated the effectiveness or efficacy of an intervention and reported an outcome or outcomes related to utilisation (prescribing

or dispensing) of generic drugs regardless of indication, setting or type of healthcare system. One reviewer examined the search results to identify potentially relevant reports. Full texts of potentially relevant reports were assessed for inclusion by two reviewers independently. Any disagreements were resolved by discussion and if necessary by involving a third reviewer.

Essential details of included reports were extracted using a simple data extraction form. These included the stated objectives, inclusion criteria, period covered by the search, interventions in included studies, main results and authors' conclusions.Data were extracted by one reviewer and checked by a second. The results were synthesised narratively and used to guide searching of the primary literature. In particular, interventions considered to be adequately covered by existing synthesised evidence were excluded from the rapid review of primary literature.

Rapid review of primary literature

Selection of studies

For the second stage, the previous search strategy described above was adapted for use in databases containing primary studies. We searchedPubMed, MEDLINE, MEDLINE In-Process, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index of Nursing and Allied Health (CINAHL), EMBASE, Health Management Information Consortium (HMIC) and PsycINFOfor studies published in English language during the period between 1985 and May 2013 (see supplementary).

Primary studies evaluating interventions designed to promote prescribing and/or dispensing of generic drugs were included.The main focus was interventions applied to individuals but interventions at the group (e.g. general practice) level were also eligible.Studies which looked at financial incentives as a main intervention were excluded as there were already reviews covering those aspects in generic prescribing. We excluded interventions considered not applicable in UK NHS settings andalso generic substitution because the Department of Health decided after a consultation exercise not to introduce such a policy.Randomised or quasi-randomised controlled trials, controlled before-and-after (CBA) studies and interrupted time-series (ITS), based on Cochrane EPOC (Effective Practice and Organisation of Care) Groupdefinitions, were eligible. The primary outcome was any measure of rate of prescribing or dispensing of generic drugs (relative to comparator group or change over time). Studies of barriers and facilitators of generic prescribing were also included but this will be reported elsewhere (a full report is available from the authors).

Records were initially screened by one reviewer to remove obviously irrelevant material, the remaining records and full papers were screened independently by two reviewers. Any disagreements were discussed with a third reviewer.

Data extraction and quality assessment

Data on objectives, setting, study design, participants, details of the intervention(s) and results/conclusions related to rates of generic prescribing/dispensing were extracted.Risk of bias was assessed using the criteria of the Cochrane EPOC Group. This was undertaken by one reviewer andchecked by a second; disagreements were resolved by discussion.

Methods of synthesis

The substantial heterogeneity of interventions and method across studies precluded meta-analysis and we therefore reported in a narrative synthesis. Studies were grouped by type of intervention or interventions.

Results

Mapping of synthesised evidence

The search identified 356 potentially relevant references:40 full papers were ordered; 10systematic reviews (9 reviews and one overview of reviews) which evaluated interventions such as financial incentives, prescribing policies, cost sharing, use of computers/IT, educational interventions, audit and feedback (Table 1).

Most of the reviews had broad objectives and did not focus specifically on interventions targeted at increasing rates of generic prescribing, for example they looked at prescribing behaviour in general rather than specifically generic prescribing. As a result there was often limited synthesis and discussion of the outcomes related to generic prescribing. This made it difficult to interpret the extent of the impact of the intervention on generic drug use in some studies.

Only two reviews had a reasonable volume of primary studies reporting generic prescribing outcomes.[6, 7]The most informative review for our research question and the UK specific focus was a Cochrane review evaluating the effect of prescribing policies using financial incentives. [6] There was evidence across all the studies included in the review of an increase in generic prescribing with fundholding, though this was not statistically significant in all the studies. In the controlled before and after studies the increase ranged from 8.8% to 13.4% at 12 months and between 4% and 17.2% at 24 months. In one controlled interrupted time series there was a 15% increase in generic prescribing (range -43.7% to 190.5%) at 12 months; in a second study using the same design there was an 18.3% increase (range 13.6% to 23%). The authors reported that budgeting funds to a group of or individual physicians (i.e. giving them financial responsibility for their own budget) increased the use of generic drugs. [6] However, the majority of studies had serious limitations and the authors cautioned that the results should be interpreted with care.[6]

The second review with a strong focus on generic prescribing, which was less relevant to the UK NHS, focused on policy intervention in low and middle income countries. The review found insufficient evidence to determine which pro-generic policies increase utilisation of generic medicines in this setting.[7] The remainder of the reviews were more specific to the US healthcare system and less relevant to the UK NHS. In addition, six of the reviews contained only a single primary study reporting generic prescribing outcomes.[8-13] Overall, most of the interventions considered in the reviews showed an increase in generic prescribing.

Table 1: Included systematic reviews

Study details	Literature search end date	Summary of authors' objective	Intervention
Carroll (2003)[8]	09/2002	To evaluate whether community pharmacists have the ability to influence prescribing decisions and the extent to which they do so	Pharmacist interventions
Figueiras (2001)[11]	1997	To propose effective continuing medical education strategies to improve prescribing practices	Educational strategies

Gibson (2005)[14]	04/2005	To determine whether patients respond to increased cost sharing by substituting less expensive alternatives for medications with higher levels of copayments or coinsurance	Cost-sharing
Green (2010)[12]	01/2009	To determine the effects of a pharmaceutical policy restricting the reimbursement of selected medications on drug use, health care utilization, health outcomes and costs	Policy restrictions on reimbursed drugs
Ivers (2012)[13]	09/2011	To investigate the effectiveness of audit and feedback to improve processes and outcomes of care and to examine factors that could influence intervention effectiveness	Audit and feedback
Kaplan (2012)[7]	01/2012	To inquire into the nature, extent and strength of the evidence for successful implementation of pro-generic medicines policies in low and middle income countries.	Pro-generic medicines policies
Mitchell (2001)[10]	1997	To appraise findings from studies examining the impact of computers on primary care consultations	Computer systems for use by doctors during consultations
McKibbon (2011)[9]	09/2009	To review the evidence on the impact of health information technology (IT) on all phases of the medication management process	IT used in the medication management process
Sturm (2007)[6]	08/2005	To determine the effects of prescribing policies using financial incentives for prescribers on drug use, healthcare utilisation, health outcomes and costs	Financial incentives (fundholding, drug budgets)

Rapid review of primary studies

A total of 11,690 records were identified from the searches of which 6144 records were potentially relevant for the rapid review (Figure 1). On the basis of screening title and abstracts, 99 full papers were ordered for further assessment. In addition, one paper was retrieved from hand searching, making a total of 100 full papers. Of the 100 full papers, 87 were excluded because; they did not meet the inclusion criteria, did not focus on generic prescribing or were irrelevant to the NHS. We also excluded studies of financial incentives as the main intervention as this had been adequately covered in a previous systematic review.[6] One study was unobtainable.[15]

Figure 1: Study Flow Diagram

Intervention studies

Thirteen studies met the inclusion criteria: two RCTs (one individual and one cluster randomisation);[16, 17] nine CBA;[18-26] and two ITS (one with control group).[27, 28]

Most of the studies werein a primary care setting; five were conducted in the UK.[17, 21-24] The interventions were single or multi-component, and included professional educational interventions (2 studies), physicians' collaboration with pharmacists (2 studies), electronic prescribing (2 studies), and multi-faceted interventions which also included the above interventions as well as networking, feedback and financial incentives (7 studies). Most of the control groups used usual practice or no intervention. Where reported baseline generic prescribing rates ranged from 3.12% to 69.4% in the intervention groups and 16.2% to 82% in the control groups.

Risk of bias in included intervention studies

The risk of bias results are summarised in tables 2 and 3.

Table 2: Risk of bias for RCTs and CBA studies

	1	2	3	4	5	6	7	8	9
RCTs									
Braybrook (2000)[17]	UC	H	L	H	UC	UC	L	L	-
Meyer (2001)[16]	L	L	L	UC	UC	UC	L	L	H
CBA									
Fischer (2008)[20]	H	H	L	H	H	L	L	L	L
Geoghegan (1998)[21]	H	H	L	UC	UC	L	L	L	UC
Leach (1999)[22]	H	H	L	UC	UC	L	L	L	L
Mastura (2008)[19]	H	H	H	UC	UC	H	L	L	H
Niquille (2010)[26]	H	H	UC	UC.	UC	H	L	H	-
Onion (1998)[23]	H	H	L	UC	L	L	L	L	L
Walker (2002)[24]	H	H	H	H	UC	UC	L	L	-
Wensing (2004)[25]	H	H	L	UC	L	L	L	L	H
Wensing (2009)[18]	H	H	L	UC	L	L	L	L	-

Key: 1. Sequence generation; 2. Allocation concealment; 3. Baseline measurements; 4. Baseline characteristics; 5. incomplete outcome data; 6. Blinded assessment of primary outcome; 7. Protection against contamination; 8. Selective outcome reporting; 9. Other risk of bias
H=high, L=low, UC=unclear

Table 3: Risk of bias for ITS studies

	1	2	3	4	5	6	7
Lopez-Picazo Ferrer (2002)[28]	UC	L	L	L	UC	L	H
Stenner (2010)[27]	L	L	L	L	UC	L	-

Key: 1. Intervention independent of other changes; 2. Shape of intervention effect; 3. Intervention unlikely to affect data collection; 4. Knowledge of allocated intervention adequately prevented; 5. Incomplete outcome data; 6. Selective outcome reporting; 7. Other risk of bias.
H=high, L=low, UC=unclear

Table 4: Characteristics of intervention studies

Study details Country/setting	Populations	Intervention	Control
Cluster RCT			
Braybrook (2000)[17] UK/ Primary care	General medical practices contracted to Gwent Health Authority (September 1993 to March 2004)	Active feedback (N= 34 practices): Visits from pharmaceutical prescribing adviser to present prescribing analysis and cost (PACT) data concerning NSAID use and to promote prescribing review.	Passive feedback (N=32 practices): Practice specific prescribing analysis workbook containing similar information to the intervention. Reference group (N=22 practices): Received no information on NSAIDs from the prescribing adviser
RCT			
Meyer (2001) [16] South Africa/ Primary health care clinics	Primary health care nurses in the Northern Province of South Africa (1997)	4-day effective prescribing training workshops provided by 24 provincial trainers who had previously received a generic training-of-trainers course and one week effective prescribing course. The effective prescribing training used the WHO annual Guide to Good Prescribing as a framework and problem-based learning methods were used. N=12 primary health care clinics randomised (11 analysed)	No training N=12 primary health care clinics randomised (11 analysed)
CBA			

Fischer (2008)[20] USA/ Community-based practices	Clinicians from community-based practices from Massachusetts (2003- 2005)	E-prescription with FDS (formulary decision support); E-prescription system (Pocket Script) identifies preferred medications, often generic medications N=1198 clinicians (clinicians needed to write at least 1e-priscriptions)	Unenrolled prescribers (Clinicians who did not use e-prescription) N= 34453 clinicians
Geoghegan (1998)[21] UK/ Primary care	General practices(GP) in St Helens and Knowsley	Prescribing meetings (at least six meeting a year) held between local GPs and community pharmacists, with agenda determined by GPs and pharmacists N=8 practices	Practices not participating in meetings N=50 practices
Leach (1999)[22] UK/ Primary care	Pharmacists and GP (general practitioners) practices in Dudley health authority	Prescribing advice to local GP from community pharmacists who had received relevant additional training (each practice received 4 visits a year from their community pharmacist) N= 5 practices (11 partners)	All remaining GP practices from the same health authority N=58 practices (151 partners)
Mastura (2008)[19] Malaysia/ Health clinic	Medical officers from government health clinics in Negeri Sembilan (2004)	Group academic detailing N=5 medical officers (1 clinic, 1848 prescriptions)	No intervention N=4 medical officers (1 clinic, 1525 prescriptions)
Niquille (2010)[26] Switzerland/ Primary care	General practices in the Swiss Canton of Fribourg who were non-dispensing physicians (1999-2007)	Quality circles (N=6 circles; 6 pharmacists and 24 GPs) Groups were moderated by specifically trained pharmacists (intervention included networking, feedback, interdisciplinary continuing education).	No intervention (N= 79 to 753 GPs each year since 1999)

Onion (1998)[23] UK/ Primary care	General practitioners (GP) in Wirral Health Authority (1992-1993)	N=10 practices Based on Ford's motivational systems theory. Included financial incentive; standard setting for improvement; interactive education; agreed performance standards for cost savings and clinical audit	No intervention (N=10 practices)
Walker (2002)[24] UK/ Primary care	General Practitioners involved in a commissioning group pilot in Southern Derbyshire (1997 – 1999)	N=9 practices; 36 GPs Pharmaceutical adviser 1 day a week for a year. Intervention included practice comparison feedback, peer review meetings, and prescribing recommendations.	No intervention (N=9 practices; 44 GPs)
Wensing (2004)[25] Germany/ Primary care	Primary care doctors from the Sachsen-Anhalt region, mainly from single-handed practices (1996-1998)	Quality circles (N=10 circles; 90 GPs) Groups were moderated by specifically trained primary care physicians. Intervention included educational session and structured feedback on individual prescribing practices.	No intervention (N=87 GPs): Random sample of physicians in the same region
Wensing (2009)[18] Germany/ Primary care	Primary care physicians (GPs) from 3 regions (2001-2003)	Quality circles (N=152 circles; 1090 GPs) Nine meetings. Intervention included provision of evidence based information and repeated feedback on individual prescribing patterns).	No intervention (N=2090 GPs): Random sample of physicians in the same region
ITS			
Lopez-Picazo (2002)[28]	Primary care teams from four of the six health areas of	N=45 practices; 339 GPs Each individual received information about individual, team and health district prescribing	N/A

Spain/ Primary care	Murcia (1998-2000)	behaviour; regularly updated information on generic drugs; up to three clinical outreach sessions with each primary care team; and specific generic prescribing goals and financial incentives to achieve the goals.	
Stenner (2010) [27] USA/ Vanderbilt Medical Group's outpatient clinics	Health care practitioners at a single medical centre, Vanderbilt University Medical Centre (VUMC) (2005-2008)	E prescribing system(Rx-Star) Changes were made to how medications were displayed on the current e-prescribing system; available generic formulations were displayed in a larger bolder font and were listed above brand name medications regardless of whether the practitioner searched for generic or brand name N=1.1 million electronic prescriptions from 2000 unique prescribers	Hand-written prescriptions that were filled at a single VUMC outpatient pharmacy (without e-prescribing, non Rx-Star) N=4456 randomly sampled prescriptions

NA=Not applicable

Narrative synthesis of intervention studies

Educational interventions

One CBA [19] and one RCT[16], both had methodological limitations, evaluated an educational interventions.There was a statistically significant increase in use of generic drugs for upper respiratory tract infection at three months follow-upin the RCT (p<0.05).[16]However, the authors reported that only 30 prescriptions per clinic were analysed retrospectively and it was unclear how they selected prescriptions for analysis. [16]In the CBA study, the proportion of prescriptions using the brand name reduced in the intervention group compared to control but there was a very strong imbalance at baseline(Intervention: Pre 33.9%, Post 19%; Control: Pre 82%; post 88.1%).[19]Overall, these studies suggest that educational interventions may be able to increase generic prescribing rates but limitations in methodology and differences in setting, as well as the small number of studies, limit the conclusions that can be drawn from them.

Physicians' collaboration with pharmacists

Two CBA studies evaluated the effectiveness of pharmacists working with General Practitioners (GPs).[21, 22] There was some baseline imbalance in one study.[22] Both studies showed improvement in generic prescribing rates, though in one study this was not statistically significant (p=0.338)[21]. In the second study there was a mean increase over baseline in total generic prescribing in the intervention group compared with control: 9/1000 at 3 months (P > 0.05), 10/1000 at 6 months (P > 0.05), 35/1000 at 12 months (P <0.01).[22] The differing results of these two studies together with their relatively weak design provide limited evidence as to whether collaboration between physicians and pharmacists can improve generic prescribing rates.

Electronic prescribing (e-prescribing)

Two studies (one CBA and one ITS),conducted in the USA, reported the effect of an e-prescribing system which identified generic medications.[20, 27] The risk of bias was relatively low in the ITS study whereasin the CBA study there were slight baseline imbalances. Both studies reported an increase in generic prescribing with e-prescribing when compared to control. In the ITS the proportion of generic prescribing increased from baseline in the intervention group (pre 32% to post 50%) and also very slightly increased in the control group (pre 29% to post 31% of hand-written prescriptions). The proportion of generic prescribing was still higher in intervention group compared to control after two years post intervention (p<0.0001) and increased significantly in every speciality with e-prescribing (range 11.8% to 62.5%).[27]

Similarly, the CBA study reported that the e-prescription group increased their generic prescribing from baseline compared to control (absolute change 3.7% vs. 2.6%). After adjusting for baseline differences between prescribers and for changes over time e-prescription corresponded to a 3.3% increase in generic prescribing.[20]

However, the relevance of this evidence to the UK is uncertain given the differences between the US and UK health systems and the fact that e-prescribing systems are already widespread.

Multi-faceted interventions

Seven studies examined multi-component interventions;[17, 18, 23-26,28] five CBA studies, one cluster RCT and one ITS.

In three studies (one cluster RCT and two CBA), a major component of the intervention was meetings between GPs and pharmacists who were giving regular feedback and prescribing recommendations.[17, 24, 26] All three studies had high or unclear risk of bias for most criteria. Two were conducted in the UK.[17, 24] One study reported no significant increase in the percentage of overall

generic drugs compared to control (p=0.17) [24] whereas the other two studies[17, 26] reported increases in generic prescribing in the intervention group.One CBA study reported that the intervention group was always higher than control for the five main cardiovascular classes of drugs for 3 years but the difference between the two groups reduced over time in each of the drug classes.[26]The cluster RCT study reported that active and passive feedback increased generic prescribing of (non-steroidal anti-inflammatory drugs (NSAIDs) compared to the reference group (pre and post differences in active, passive and reference group: 7%, 6%, and 4%).[17]

Two CBA studies, involving 90 and 1090 GPs from Germany, used quality circles which were moderated by primary care doctors and involved structured feedback on individual prescribing patterns and educational sessions.[18, 25] Both studies were high risk of bias in randomisation and allocation concealment and unclear risk in baseline characteristics. The 2009 study,[18] which involved 1090 GPs, reported no significant difference in prescribing generic drugs compared to control whereas the 2004 study,[25] which involved 90 GPs, reported significant increase in the percentage of generic prescribing in the intervention group (OR 1.10, 95%CI 1.08 to 1.13).

One CBA study which involved GPs from 10 practices from the UK used multiple interventions which included financial incentives, setting of standards for improvement, interactive education, agreed performance for cost savings and clinical audit.[23] The risk of bias was high for randomisation and allocation concealment, and unclear for baseline characteristics. The authors reported that the proportion of generic prescribing increased in the intervention group by 5% compared with the control(OR 1.22, 95% CI 1.18 to 1.28, p<0.0001).However, differences in the two groups started to decline after a further three months.[23]

Finally we included an ITS study which involved 339 family physicians from 45 primary care teams from Spain who received personalised information regarding prescribing behaviour, updated information cards on generic drugs and a letter, clinical outreach session with each primary care team, specific prescribing goal and financial incentives.[28] The risk of bias was low for most criteria, however it was unclear whether the interventions were independent of other changes. The study reported increased generic prescribing in the intervention group. The mean percentage of generic prescriptions for the 3 month period immediately before the intervention was 2.79% and for the 3 months immediately following the end of the intervention was 17.63%; absolute improvement was 14.84% and relative improvement was 15.27%.[28]

Discussion

Summary of main results

Our objective was to identify and summarise the research evidence on interventions aimed at improving generic prescribing rates. We took a two stage approach: first we identified and summarised existing synthesised evidence. Second, as little synthesised evidence is available, we conducted a rapid review of the primary literature on interventions to improve rates of generic prescribing.

Only two systematic reviews focused specifically on generic prescribing behaviours. The evidence from a Cochrane review suggests possible benefits of financial incentives to support generic prescribing.[6]Many areas currentlyuse prescribing incentive schemes to support cost-effective prescribing and this strategy is endorsed, subject to suitable safeguards, by the English Department

of Health.[29] The second review with a strong focus on generic prescribing, which was less relevant to the NHS, focused on policy intervention in low and middle income countries.

We identified thirteen primary studies which evaluated the effects of an intervention to improve generic drug utilisation. Two studies evaluated an educational intervention and showed an increase in the percentage of overall prescribing of generic drugs; two studies which evaluated the effect of physicians collaborating with pharmacists showed improvement in generic prescribing rates, though in one study this was not statistically significant; and two studies from the USA which evaluated e-electronic prescribing showed improvements in generic prescribing. Seven studies used multi-component interventions. The interventions included various combinations of education, collaborations with pharmacists, quality circles, financial incentives and feedback on prescribing practices.

Five of the seven studies of multiple component interventions reported significant improvements in rates of generic prescribing associated with the intervention. However, only one of these was a randomised trial[17] and that trial was deemed to be at relatively high risk of bias. Similarly, two out of three studies with relatively similar interventions from the UK reported positive results, though one was not statistically significant.[17, 24] One study[23] differed from the others by incorporating financial incentives (which are considered possibly effective based on systematic review evidence) and by being based on a specific theory of behaviour change. A major limitation of these studies is that they were conducted between 1998 and 2002, so their relevance to the present-day NHS may be questionable. In addition, only five primary studies out of 13 were from the UK. Overall, the evidence on multiple component interventions, as with that for specific single interventions appears too weak and heterogeneous to provide clear guidance on how generic prescribing might be further improved.

Strengths and limitations of the review process

We searched several different databases for published as well as unpublished studies. The study quality was assessed systematically and taken into consideration in the synthesis. Appropriate methods were employed to minimise reviewer bias and error in all stages of the review process. We included only English-language studies for the rapid review, both for practical reasons related to the resources available, and because we were primarily interested in studies which are relevant to the UK NHS setting. While this might have led to the risk of relevant studies being overlooked, in practice the risk is likely to be small.

A feature of this project was the adoption of a two-stage approach, with an initial mapping of synthesised evidence followed by a review of primary studies guided by the results of the first stage.Examination of the available systematic reviews of interventions to improve prescribing allowed us to identify financial incentives as an intervention with a reasonable evidence base of research relevant to the UK NHS. This in turn reduced the work involved in the review of primary literature.

Our main focus was on the effectiveness of interventions regardless of setting but we recognise that the context for generic prescribing differs widely between health systems. In particular, low and middle income countries (LMICs) have very different issues to developed countries like the UK. Given the limited evidence found, we did not exclude studies conducted in LMICs from the synthesis. However, only one systematic review and two primary studies came into this category and excluding studies from LMICs is unlikely to have affected our conclusions.

Limitations of the evidence base

Even though most interventions had positive results various methodological weaknesses especially in randomisation and allocation concealment may have biased their findings.Only two of the primary studies included in our rapid review were RCTs.[17]In addition most of the studies had small sample sizes.Most of the studies attracted participants who had expressed an interest in generic prescribing or who were already involved in fundholding; therefore, they have had increased motivation to save money by prescribing generic drugs which could overestimate the effects. In addition, the long term effects on generic prescribing were not reported, so it was unclear whether the observed effects were sustainable in the longer run. However, it is arguable that studies reporting benefit up to 12 months suggest that the effects can be sustained.

Implications for policy and practice

Generic prescribing in the UK NHS is already at a high level and achievement of 100% generic prescribing is neither feasible nor desirable. It is well established that thoughtless implementation of policy initiatives to replace branded drugs by generic equivalents may result in confusion for patients or in some cases actual harm.[30, 31]Indeed, the Better Care, Better Value (BCBV) indicators, introduced to support prescribing of generic proton pump inhibitors, statins and ACE inhibitors are apparently no longer published,[32] possibly because nearly all statins and proton pump inhibitors (PPIs) are available as generics, as well as an appreciable number of angiotensin receptor blockers (ARBs).

A paper published too late for consideration for inclusion in our review outlines measures in the UK (Scotland) to encourage prescribing of generic drugs using the INN (international non-proprietary name).[33] Some European countries have systems of compulsory INN prescribing,[34] but as noted above this option has been ruled out by the Department of Health. A further issue in Europe with limited relevance for the UK is the availability of branded generic drugs in some countries. Interventions to promote the use of these agents are similar to those for generic drugs generally, e.g. generic substitution,[35] and educational initiatives. In some healthcare systems patients may be required to meet the additional costs themselves if they are prescribed a product more expensive than the recommended (reference priced) generic drug.[36]

The main focus in the UK has been on encouraging use of generics versus patented products within a class or related class. This assumes that the products are similar in all or nearly all patients at appropriate doses, as in the drug classes covered by the BCBV indicators.There are classes of drugs for which generic forms are available but this assumption does not hold, for example atypical antipsychotics. This is because individual antipsychotic drugs differ in their adverse effect profiles and clinicians need to select the most appropriate agent based on the patient's characteristics and preferences. A recent non-systematic review found that the availability of generic risperidone in Scotland had no appreciable effect on prescribing patterns, although the authors suggested that there was potential to increase prescribing of generic atypical antipsychotics through educational activities.[37]

Evidence from a Cochrane systematic review suggests possible benefits of financial incentives to support generic prescribing.[6] The UK studies included in the review mainly relate to GP fundholding which is no longer used. Many areas use prescribing incentive schemes to support cost-effective prescribing.[29] Incentive schemes may focus on specific drugs or drug classes in accordance with local conditions.

The review of primary studies suggested that a range of interventions may be effective in increasing rates of generic prescribing. However, limitations in the evidence base make it difficult to identify any specific intervention or combination of interventions particularly suitable for implementation in the contemporary NHS setting. Decision-makers will need to consider which interventions appear most suitable to their specific setting. They may also want to consider whether the likely benefits of an intervention will outweigh its costs given the high levels of generic prescribing achieved by existing measures.

A number of systematic reviews of better quality evidence have shown modest absolute increases in desired health professionalbehaviours associated with interventions like audit and feedback, educational meetings and outreach and reminder systems.[13, 38] Given the relative consistency of results, this evidence in conjunction with our review findings could help in estimating the likely impact of a proposed intervention on generic prescribing behaviour.

Prescribing restrictions or removal of products from reimbursement lists to encourage generic prescribing has been used in some European countries but not in the UK. An example is switching from patented to generic statins in Norway[39]and Finland.[40]A related approach is to lift restrictions for generic forms only, as was done for angiotensin receptor blockers in some European countries when generic losartan became available.[41] However, such policies are unlikely to be applied in the UK and as whole health system policy interventions they are outside the scope of this review.

Implications for research

Although high quality RCTs would improve the evidence base, it is unclear whether such studies would be justified, as the sample size required to demonstrate a benefit over current best practice would be large and the absolute improvement would be small. However, trials of specific interventions targeted at practices or individuals with particularly low levels of generic prescribing could be considered. Such trials should evaluate interventions that have proved successful in changing other types of behaviour and are based on a robust theory of behaviour change.

Given the existence of substantial variation between areas and individual general practices, further research may be helpful to explore the reasons for this. Research could focus on specific highly prescribed drugs with generic forms available (e.g. statins) and use a qualitative or mixed methods design.

Conclusions

Although several interventions look promising, complex interventions, methodological weaknesses and conflicting results limit the validity and applicability of the findings. In particular most of the available studies were conducted with baseline rates of generic prescribing significantly lower than the NHS is currently achieving. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

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CONTRIBUTORSHIP STATEMENT

MH designed the search strategy and performed the literature search. TMB, DC and CMcD screened the titles and abstracts and managed the references. All 3 reviewers (TMB, DC and CMcD) screened the retrieved papers against inclusion criteria and independently performed the data extraction and quality evaluation assessment for the review. All 3 reviewers interpreted the results. All authors have approved the manuscript and given approval for it to be published.

COMPETING INTERESTS

None

DATA SHARING STATEMENT

Extra data can be accessed by e-mailing duncan.chambers@york.ac.uk

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Title: Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review

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ABSTRACT

Objective: To summarise evidence on the effectiveness of behaviour change interventions to encourage prescribing of generic forms of prescription drugs where clinically appropriate in the UK NHS and similar settings.

Design: systematic review

Search strategy: We conducted a rapid evidence synthesis in two stages: Firstly, we searched databases such as the Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE), for systematic reviews of interventions that reported outcomes related to utilisation of generic drugs. For the second stage, we searched several databases including MEDLINE and EMBASE to identify primary studies of any interventions not adequately covered by systematic reviews.

Data extraction and quality assessment: Data were extracted into a standardised data extraction form. Standardised quality assessment tools were used to assess study quality. Two reviewers were involved in data extraction and quality assessment.

Results: Ten reviews were included for the initial evidence synthesis but most were of limited usefulness to our focused review question. One review evaluated the effect of prescribing policies using financial incentives and showed an increase in generic prescribing. Thirteen primary studies of other interventions were included for the rapid review. Two studies showed an increase in percentage of overall generic prescribing with an educational intervention; two studies showed improvement in generic prescribing rates when physicians collaborated with pharmacists, though in one study this was not statistically significant; two US studies showed improvements in generic prescribing with electronic prescribing. Five out of seven studies showed positive results with multi-faceted interventions.

Conclusions: The existing evidence remains insufficient to determine which behaviour change intervention or combination of interventions is most effective due to methodological weaknesses and conflicting results. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

Article Summary

'Strengths and limitations of this study'

- Appropriate use of generic medicines is important for healthcare systems to make optimum use of limited resources. In England, rates of prescribing by generic name are over 80% overall but there is evidence of variation between regions and individual prescribers.
- We have synthesised evidence from systematic and primary studies that have evaluated the effectiveness of interventions to promote generic prescribing at the level of the individual prescriber or GP practice.
- The study brings together evidence on a wide range of behaviour change interventions and identifies a number of potentially effective approaches.
- Limitations of the evidence base make it difficult to draw any firm conclusions about the relative effectiveness of different approaches. Recent evidence from UK NHS settings is particularly lacking.
- Given the uncertainty around the evidence base, decision-makers in settings where only small improvements in generic prescribing rates are likely to be achievable should take into account the practicality and costs of the intervention before implementing measures designed to further increase generic prescribing rates.

BACKGROUND

Generic medicines, which are the substitutes of original (branded) medicines with the same quality, safety and efficacy,[1] offer an interesting opportunity for governments and healthcare payers to contain escalating healthcare budgets as their prices tend to be 10–80% lower than their proprietary equivalents.[2] In England the proportion of prescriptions prescribed generically (i.e. by non-proprietary name rather than brand name) increased from 76% in 2002 to 83.6% in 2012.[3]

Despite the trend of increasing generic prescribing rates there is thought to be room for greater efficiency. In 2008 approximately 5% of medicines were prescribed by their brand name in England when there was a generic alternative available.[4] A national Audit Office report in 2007 reported that prescriptions of generic statins ~~generic statins (simvastatin and pravastatin)~~ (i.e., the use of multiple sourced simvastatin and pravastatin vs. patented Lipitor and Crestor) varied from 28% to 86% across English Primary Care Trusts.[5] More recent research has also identified marked variation in generic prescribing by GPs (for data on statin prescriptions in England, see www.prescribinganalytics.com).

In 2009, the Department of Health consulted on a proposal for the introduction of generic substitution (allowing pharmacists to fulfil a prescription for a branded medicine by dispensing a generic equivalent) in primary care in England. However, after considering the responses to the consultation, the Government decided not to progress the proposal further.[4] As an alternative it was suggested that 'other, less nationally prescriptive mechanisms for further supporting the use of generic medicines can be explored'.

We have undertaken a rapid evidence synthesis to inform decision-makers about the use of generics versus patented products and the evidence base for interventions that might be applied to increase generic prescribing at the level of the individual or small units such as general practices.

Aims/objectives

To identify and summarise relevant research evidence using existing synthesised evidence sources (systematic reviews) supplemented as necessary by a rapid systematic review of primary research. The project aims to benefit the UK NHS by increasing the accessibility of the relevant evidence and by identifying gaps that need to be filled by further research.

Methods

We conducted this rapid evidence synthesis in two stages: an initial mapping of existing sources of synthesised evidence followed by rapid systematic review of the primary research literature, for interventions not covered by previous reviews. We registered the protocol of this review on PROSPERO the international prospective register of systematic reviews (registration number CRD42013004443).

Mapping of synthesised evidence

We searched the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment (HTA) database and Health Systems Evidence for the systematic reviews to map the existing sources of synthesised evidence. Terms relating to prescribing were combined using the Boolean operator AND with terms for generic drugs. No date or language limits were applied.

Systematic reviews, HTA reports and overviews were included if they evaluated the effectiveness or efficacy of an intervention and reported an outcome or outcomes related to utilisation (prescribing or dispensing) of generic drugs regardless of indication, setting or type of healthcare system. One reviewer examined the search results to identify potentially relevant reports. Full texts of potentially relevant reports were assessed for inclusion by two reviewers independently. Any disagreements were resolved by discussion and if necessary by involving a third reviewer.

Essential details of included reports were extracted using a simple data extraction form. These included the stated objectives, inclusion criteria, period covered by the search, interventions in included studies, main results and authors' conclusions. Data were extracted by one reviewer and checked by a second. The results were synthesised narratively and used to guide searching of the primary literature. In particular, interventions considered to be adequately covered by existing synthesised evidence were excluded from the rapid review of primary literature.

Rapid review of primary literature

Selection of studies

For the second stage, the previous search strategy described above was adapted for use in databases containing primary studies. We searched PubMed, MEDLINE, MEDLINE In-Process, Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index of Nursing and Allied Health (CINAHL), EMBASE, Health Management Information Consortium (HMIC) and PsycINFO for studies published in English language during the period between 1985 and May 2013 (see supplementary).

Primary studies evaluating interventions designed to promote prescribing and/or dispensing of generic drugs were included. The main focus was interventions applied to individuals but interventions at the group (e.g. general practice) level were also eligible. Studies which looked at financial incentives as a main intervention were excluded as there were already reviews covering those aspects in generic prescribing. We excluded interventions considered not applicable in UK NHS settings and also generic substitution because the Department of Health decided after a consultation exercise not to introduce such a policy. Randomised or quasi-randomised controlled trials, controlled before-and-after (CBA) studies and interrupted time-series (ITS), based on Cochrane EPOC (Effective Practice and Organisation of Care) Group definitions, were eligible. The primary outcome was any measure of rate of prescribing or dispensing of generic drugs (relative to comparator group or change over time). Studies of barriers and facilitators of generic prescribing were also included but this will be reported elsewhere (a full report is available from the authors).

Records were initially screened by one reviewer to remove obviously irrelevant material, the remaining records and full papers were screened independently by two reviewers. Any disagreements were discussed with a third reviewer.

Data extraction and quality assessment

Data on objectives, setting, study design, participants, details of the intervention(s) and results/conclusions related to rates of generic prescribing/dispensing were extracted. Risk of bias was assessed using the criteria of the Cochrane EPOC Group. This was undertaken by one reviewer and checked by a second; disagreements were resolved by discussion.

Methods of synthesis

The substantial heterogeneity of interventions and method across studies precluded meta-analysis and we therefore reported in a narrative synthesis. Studies were grouped by type of intervention or interventions.

Results

Mapping of synthesised evidence

The search identified 356 potentially relevant references:40 full papers were ordered; 10systematic reviews (9 reviews and one overview of reviews) which evaluated interventions such as financial incentives, prescribing policies, cost sharing, use of computers/IT, educational interventions, audit and feedback (Table 1).

Most of the reviews had broad objectives and did not focus specifically on interventions targeted at increasing rates of generic prescribing, for example they looked at prescribing behaviour in general rather than specifically generic prescribing. As a result there was often limited synthesis and discussion of the outcomes related to generic prescribing. This made it difficult to interpret the extent of the impact of the intervention on generic drug use in some studies.

Only two reviews had a reasonable volume of primary studies reporting generic prescribing outcomes.[6, 7]The most informative review for our research question and the UK specific focus was a Cochrane review evaluating the effect of prescribing policies using financial incentives. [6] There was evidence across all the studies included in the review of an increase in generic prescribing with fundholding, though this was not statistically significant in all the studies. In the controlled before and after studies the increase ranged from 8.8% to 13.4% at 12 months and between 4% and 17.2% at 24 months. In one controlled interrupted time series there was a 15% increase in generic prescribing (range -43.7% to 190.5%) at 12 months; in a second study using the same design there was an 18.3% increase (range 13.6% to 23%). The authors reported that budgeting funds to a group of or individual physicians (i.e. giving them financial responsibility for their own budget) increased the use of generic drugs. [6] However, the majority of studies had serious limitations and the authors cautioned that the results should be interpreted with care.[6]

The second review with a strong focus on generic prescribing, which was less relevant to the UK NHS, focused on policy intervention in low and middle income countries. The review found insufficient evidence to determine which pro-generic policies increase utilisation of generic medicines in this setting.[7] The remainder of the reviews were more specific to the US healthcare system and less relevant to the UK NHS. In addition, six of the reviews contained only a single primary study reporting generic prescribing outcomes.[8-13] Overall, most of the interventions considered in the reviews showed an increase in generic prescribing.

Table 1: Included systematic reviews

Study details	Literature search end date	Summary of authors' objective	Intervention
Carroll (2003)[8]	09/2002	To evaluate whether community pharmacists have the ability to influence prescribing decisions and the extent to which they do so	Pharmacist interventions
Figueiras (2001)[11]	1997	To propose effective continuing medical education strategies to improve prescribing practices	Educational strategies

Gibson (2005)[14]	04/2005	To determine whether patients respond to increased cost sharing by substituting less expensive alternatives for medications with higher levels of copayments or coinsurance	Cost-sharing
Green (2010)[12]	01/2009	To determine the effects of a pharmaceutical policy restricting the reimbursement of selected medications on drug use, health care utilization, health outcomes and costs	Policy restrictions on reimbursed drugs
Ivers (2012)[13]	09/2011	To investigate the effectiveness of audit and feedback to improve processes and outcomes of care and to examine factors that could influence intervention effectiveness	Audit and feedback
Kaplan (2012)[7]	01/2012	To inquire into the nature, extent and strength of the evidence for successful implementation of pro-generic medicines policies in low and middle income countries.	Pro-generic medicines policies
Mitchell (2001)[10]	1997	To appraise findings from studies examining the impact of computers on primary care consultations	Computer systems for use by doctors during consultations
McKibbon (2011)[9]	09/2009	To review the evidence on the impact of health information technology (IT) on all phases of the medication management process	IT used in the medication management process
Sturm (2007)[6]	08/2005	To determine the effects of prescribing policies using financial incentives for prescribers on drug use, healthcare utilisation, health outcomes and costs	Financial incentives (fundholding, drug budgets)

Rapid review of primary studies

A total of 11,690 records were identified from the searches of which 6144 records were potentially relevant for the rapid review (Figure 1). On the basis of screening title and abstracts, 99 full papers were ordered for further assessment. In addition, one paper was retrieved from hand searching, making a total of 100 full papers. Of the 100 full papers, 87 were excluded because; they did not meet the inclusion criteria, did not focus on generic prescribing or were irrelevant to the NHS. We also excluded studies of financial incentives as the main intervention as this had been adequately covered in a previous systematic review.[6] One study was unobtainable.[15]

Figure 1: Study Flow Diagram

Intervention studies

Thirteen studies met the inclusion criteria: two RCTs (one individual and one cluster randomisation);[16, 17] nine CBA;[18-26] and two ITS (one with control group).[27, 28]

Most of the studies were in a primary care setting; five were conducted in the UK.[17, 21-24] The interventions were single or multi-component, and included professional educational interventions (2 studies), physicians' collaboration with pharmacists (2 studies), electronic prescribing (2 studies), and multi-faceted interventions which also included the above interventions as well as networking, feedback and financial incentives (7 studies). Most of the control groups used usual practice or no intervention. Where reported baseline generic prescribing rates ranged from 3.12% to 69.4% in the intervention groups and 16.2% to 82% in the control groups.

Risk of bias in included intervention studies

The risk of bias results are summarised in tables 2 and 3.

Table 2: Risk of bias for RCTs and CBA studies

	1	2	3	4	5	6	7	8	9
RCTs									
Braybrook (2000)[17]	UC	H	L	H	UC	UC	L	L	-
Meyer (2001)[16]	L	L	L	UC	UC	UC	L	L	H
CBA									
Fischer (2008)[20]	H	H	L	H	H	L	L	L	L
Geoghegan (1998)[21]	H	H	L	UC	UC	L	L	L	UC
Leach (1999)[22]	H	H	L	UC	UC	L	L	L	L
Mastura (2008)[19]	H	H	H	UC	UC	H	L	L	H
Niquille (2010)[26]	H	H	UC	UC.	UC	H	L	H	-
Onion (1998)[23]	H	H	L	UC	L	L	L	L	L
Walker (2002)[24]	H	H	H	H	UC	UC	L	L	-
Wensing (2004)[25]	H	H	L	UC	L	L	L	L	H
Wensing (2009)[18]	H	H	L	UC	L	L	L	L	-

Key: 1. Sequence generation; 2. Allocation concealment; 3. Baseline measurements; 4. Baseline characteristics; 5. incomplete outcome data; 6. Blinded assessment of primary outcome; 7. Protection against contamination; 8. Selective outcome reporting; 9. Other risk of bias
H=high, L=low, UC=unclear

Table 3: Risk of bias for ITS studies

	1	2	3	4	5	6	7
Lopez-Picazo Ferrer (2002)[28]	UC	L	L	L	UC	L	H
Stenner (2010)[27]	L	L	L	L	UC	L	-

Key: 1. Intervention independent of other changes; 2. Shape of intervention effect; 3. Intervention unlikely to affect data collection; 4. Knowledge of allocated intervention adequately prevented; 5. Incomplete outcome data; 6. Selective outcome reporting; 7. Other risk of bias.
H=high, L=low, UC=unclear

Table 4: Characteristics of intervention studies

Study details Country/setting	Populations	Intervention	Control
Cluster RCT			
Braybrook (2000)[17] UK/ Primary care	General medical practices contracted to Gwent Health Authority (September 1993 to March 2004)	Active feedback (N= 34 practices): Visits from pharmaceutical prescribing adviser to present prescribing analysis and cost (PACT) data concerning NSAID use and to promote prescribing review.	Passive feedback (N=32 practices): Practice specific prescribing analysis workbook containing similar information to the intervention. Reference group (N=22 practices): Received no information on NSAIDs from the prescribing adviser
RCT			
Meyer (2001) [16] South Africa/ Primary health care clinics	Primary health care nurses in the Northern Province of South Africa (1997)	4-day effective prescribing training workshops provided by 24 provincial trainers who had previously received a generic training-of-trainers course and one week effective prescribing course. The effective prescribing training used the WHO annual Guide to Good Prescribing as a framework and problem-based learning methods were used. N=12 primary health care clinics randomised (11 analysed)	No training N=12 primary health care clinics randomised (11 analysed)
CBA			

Fischer (2008)[20] USA/ Community-based practices	Clinicians from community-based practices from Massachusetts (2003- 2005)	E-prescription with FDS (formulary decision support); E-prescription system (Pocket Script) identifies preferred medications, often generic medications N=1198 clinicians (clinicians needed to write at least 1e-priscriptions)	Unenrolled prescribers (Clinicians who did not use e-prescription) N= 34453 clinicians
Geoghegan (1998)[21] UK/ Primary care	General practices(GP) in St Helens and Knowsley	Prescribing meetings (at least six meeting a year) held between local GPs and community pharmacists, with agenda determined by GPs and pharmacists N=8 practices	Practices not participating in meetings N=50 practices
Leach (1999)[22] UK/ Primary care	Pharmacists and GP (general practitioners) practices in Dudley health authority	Prescribing advice to local GP from community pharmacists who had received relevant additional training (each practice received 4 visits a year from their community pharmacist) N= 5 practices (11 partners)	All remaining GP practices from the same health authority N=58 practices (151 partners)
Mastura (2008)[19] Malaysia/ Health clinic	Medical officers from government health clinics in Negeri Sembilan (2004)	Group academic detailing N=5 medical officers (1 clinic, 1848 prescriptions)	No intervention N=4 medical officers (1 clinic, 1525 prescriptions)
Niquille (2010)[26] Switzerland/ Primary care	General practices in the Swiss Canton of Fribourg who were non-dispensing physicians (1999-2007)	Quality circles (N=6 circles; 6 pharmacists and 24 GPs) Groups were moderated by specifically trained pharmacists (intervention included networking, feedback, interdisciplinary continuing education).	No intervention (N= 79 to 753 GPs each year since 1999)

Onion (1998)[23] UK/ Primary care	General practitioners (GP) in Wirral Health Authority (1992-1993)	N=10 practices Based on Ford's motivational systems theory. Included financial incentive; standard setting for improvement; interactive education; agreed performance standards for cost savings and clinical audit	No intervention (N=10 practices)
Walker (2002)[24] UK/ Primary care	General Practitioners involved in a commissioning group pilot in Southern Derbyshire (1997 – 1999)	N=9 practices; 36 GPs Pharmaceutical adviser 1 day a week for a year. Intervention included practice comparison feedback, peer review meetings, and prescribing recommendations.	No intervention (N=9 practices; 44 GPs)
Wensing (2004)[25] Germany/ Primary care	Primary care doctors from the Sachsen-Anhalt region, mainly from single-handed practices (1996-1998)	Quality circles (N=10 circles; 90 GPs) Groups were moderated by specifically trained primary care physicians. Intervention included educational session and structured feedback on individual prescribing practices.	No intervention (N=87 GPs): Random sample of physicians in the same region
Wensing (2009)[18] Germany/ Primary care	Primary care physicians (GPs) from 3 regions (2001-2003)	Quality circles (N=152 circles; 1090 GPs) Nine meetings. Intervention included provision of evidence based information and repeated feedback on individual prescribing patterns).	No intervention (N=2090 GPs): Random sample of physicians in the same region
ITS			
Lopez-Picazo (2002)[28]	Primary care teams from four of the six health areas of	N=45 practices; 339 GPs Each individual received information about individual, team and health district prescribing	N/A

Spain/ Primary care	Murcia (1998-2000)	behaviour; regularly updated information on generic drugs; up to three clinical outreach sessions with each primary care team; and specific generic prescribing goals and financial incentives to achieve the goals.	
Stenner (2010)27 USA/ Vanderbilt Medical Group's outpatient clinics	Health care practitioners at a single medical centre, Vanderbilt University Medical Centre (VUMC) (2005-2008)	E prescribing system(Rx-Star) Changes were made to how medications were displayed on the current e-prescribing system; available generic formulations were displayed in a larger bolder font and were listed above brand name medications regardless of whether the practitioner searched for generic or brand name N=1.1 million electronic prescriptions from 2000 unique prescribers	Hand-written prescriptions that were filled at a single VUMC outpatient pharmacy (without e-prescribing, non Rx-Star) N=4456 randomly sampled prescriptions

NA=Not applicable

Narrative synthesis of intervention studies

Educational interventions

One CBA [19] and one RCT[16], both had methodological limitations, evaluated an educational interventions. There was a statistically significant increase in use of generic drugs for upper respiratory tract infection at three months follow-upin the RCT (p<0.05).[16]However, the authors reported that only 30 prescriptions per clinic were analysed retrospectively and it was unclear how they selected prescriptions for analysis. [16]In the CBA study, the proportion of prescriptions using the brand name reduced in the intervention group compared to control but there was a very strong imbalance at baseline(Intervention: Pre 33.9%, Post 19%; Control: Pre 82%; post 88.1%).[19]Overall, these studies suggest that educational interventions may be able to increase generic prescribing rates but limitations in methodology and differences in setting, as well as the small number of studies, limit the conclusions that can be drawn from them.

Physicians' collaboration with pharmacists

Two CBA studies evaluated the effectiveness of pharmacists working with General Practitioners (GPs).[21, 22] There was some baseline imbalance in one study.[22] Both studies showed improvement in generic prescribing rates, though in one study this was not statistically significant (p=0.338)[21]. In the second study there was a mean increase over baseline in total generic prescribing in the intervention group compared with control: 9/1000 at 3 months (P > 0.05), 10/1000 at 6 months (P > 0.05), 35/1000 at 12 months (P <0.01).[22] The differing results of these two studies together with their relatively weak design provide limited evidence as to whether collaboration between physicians and pharmacists can improve generic prescribing rates.

Electronic prescribing (e-prescribing)

Two studies (one CBA and one ITS), conducted in the USA, reported the effect of an e-prescribing system which identified generic medications.[20, 27] The risk of bias was relatively low in the ITS study whereas in the CBA study there were slight baseline imbalances. Both studies reported an increase in generic prescribing with e-prescribing when compared to control. In the ITS the proportion of generic prescribing increased from baseline in the intervention group (pre 32% to post 50%) and also very slightly increased in the control group (pre 29% to post 31% of hand-written prescriptions). The proportion of generic prescribing was still higher in intervention group compared to control after two years post intervention (p<0.0001) and increased significantly in every speciality with e-prescribing (range 11.8% to 62.5%).[27]

Similarly, the CBA study reported that the e-prescription group increased their generic prescribing from baseline compared to control (absolute change 3.7% vs. 2.6%). After adjusting for baseline differences between prescribers and for changes over time e-prescription corresponded to a 3.3% increase in generic prescribing.[20]

However, the relevance of this evidence to the UK is uncertain given the differences between the US and UK health systems and the fact that e-prescribing systems are already widespread.

Multi-faceted interventions

Seven studies examined multi-component interventions;[17, 18, 23-26, 28] five CBA studies, one cluster RCT and one ITS.

In three studies (one cluster RCT and two CBA), a major component of the intervention was meetings between GPs and pharmacists who were giving regular feedback and prescribing recommendations.[17, 24, 26] All three studies had high or unclear risk of bias for most criteria. Two were conducted in the UK.[17, 24] One study reported no significant increase in the percentage of overall

generic drugs compared to control (p=0.17) [24] whereas the other two studies[17, 26] reported increases in generic prescribing in the intervention group. One CBA study reported that the intervention group was always higher than control for the five main cardiovascular classes of drugs for 3 years but the difference between the two groups reduced over time in each of the drug classes.[26]The cluster RCT study reported that active and passive feedback increased generic prescribing of (non-steroidal anti-inflammatory drugs (NSAIDs) compared to the reference group (pre and post differences in active, passive and reference group: 7%, 6%, and 4%).[17]

Two CBA studies, involving 90 and 1090 GPs from Germany, used quality circles which were moderated by primary care doctors and involved structured feedback on individual prescribing patterns and educational sessions.[18, 25] Both studies were high risk of bias in randomisation and allocation concealment and unclear risk in baseline characteristics. The 2009 study,[18] which involved 1090 GPs, reported no significant difference in prescribing generic drugs compared to control whereas the 2004 study,[25] which involved 90 GPs, reported significant increase in the percentage of generic prescribing in the intervention group (OR 1.10, 95%CI 1.08 to 1.13).

One CBA study which involved GPs from 10 practices from the UK used multiple interventions which included financial incentives, setting of standards for improvement, interactive education, agreed performance for cost savings and clinical audit.[23] The risk of bias was high for randomisation and allocation concealment, and unclear for baseline characteristics. The authors reported that the proportion of generic prescribing increased in the intervention group by 5% compared with the control(OR 1.22, 95% CI 1.18 to 1.28, p<0.0001).However, differences in the two groups started to decline after a further three months.[23]

Finally we included an ITS study which involved 339 family physicians from 45 primary care teams from Spain who received personalised information regarding prescribing behaviour, updated information cards on generic drugs and a letter, clinical outreach session with each primary care team, specific prescribing goal and financial incentives.[28] The risk of bias was low for most criteria, however it was unclear whether the interventions were independent of other changes. The study reported increased generic prescribing in the intervention group. The mean percentage of generic prescriptions for the 3 month period immediately before the intervention was 2.79% and for the 3 months immediately following the end of the intervention was 17.63%; absolute improvement was 14.84% and relative improvement was 15.27%.[28]

Discussion

Summary of main results

Our objective was to identify and summarise the research evidence on interventions aimed at improving generic prescribing rates. We took a two stage approach: first we identified and summarised existing synthesised evidence. Second, as little synthesised evidence is available, we conducted a rapid review of the primary literature on interventions to improve rates of generic prescribing.

Only two systematic reviews focused specifically on generic prescribing behaviours. The evidence from a Cochrane review suggests possible benefits of financial incentives to support generic prescribing.[6] Many areas currently use prescribing incentive schemes to support cost-effective prescribing and this strategy is endorsed, subject to suitable safeguards, by the English Department

of Health.[29] The second review with a strong focus on generic prescribing, which was less relevant to the NHS, focused on policy intervention in low and middle income countries.

We identified thirteen primary studies which evaluated the effects of an intervention to improve generic drug utilisation. Two studies evaluated an educational intervention and showed an increase in the percentage of overall prescribing of generic drugs; two studies which evaluated the effect of physicians collaborating with pharmacists showed improvement in generic prescribing rates, though in one study this was not statistically significant; and two studies from the USA which evaluated e-electronic prescribing showed improvements in generic prescribing. Seven studies used multi-component interventions. The interventions included various combinations of education, collaborations with pharmacists, quality circles, financial incentives and feedback on prescribing practices.

Five of the seven studies of multiple component interventions reported significant improvements in rates of generic prescribing associated with the intervention. However, only one of these was a randomised trial[17] and that trial was deemed to be at relatively high risk of bias. Similarly, two out of three studies with relatively similar interventions from the UK reported positive results, though one was not statistically significant.[17, 24] One study[23] differed from the others by incorporating financial incentives (which are considered possibly effective based on systematic review evidence) and by being based on a specific theory of behaviour change. A major limitation of these studies is that they were conducted between 1998 and 2002, so their relevance to the present-day NHS may be questionable. In addition, only five primary studies out of 13 were from the UK. Overall, the evidence on multiple component interventions, as with that for specific single interventions appears too weak and heterogeneous to provide clear guidance on how generic prescribing might be further improved.

Strengths and limitations of the review process

We searched several different databases for published as well as unpublished studies. The study quality was assessed systematically and taken into consideration in the synthesis. Appropriate methods were employed to minimise reviewer bias and error in all stages of the review process. We included only English-language studies for the rapid review, both for practical reasons related to the resources available, and because we were primarily interested in studies which are relevant to the UK NHS setting. While this might have led to the risk of relevant studies being overlooked, in practice the risk is likely to be small.

A feature of this project was the adoption of a two-stage approach, with an initial mapping of synthesised evidence followed by a review of primary studies guided by the results of the first stage. Examination of the available systematic reviews of interventions to improve prescribing allowed us to identify financial incentives as an intervention with a reasonable evidence base of research relevant to the UK NHS. This in turn reduced the work involved in the review of primary literature.

Our main focus was on the effectiveness of interventions regardless of setting but we recognise that the context for generic prescribing differs widely between health systems. In particular, low and middle income countries (LMICs) have very different issues to developed countries like the UK. Given the limited evidence found, we did not exclude studies conducted in LMICs from the synthesis. However, only one systematic review and two primary studies came into this category and excluding studies from LMICs is unlikely to have affected our conclusions.

Limitations of the evidence base

Even though most interventions had positive results various methodological weaknesses especially in randomisation and allocation concealment may have biased their findings. Only two of the primary studies included in our rapid review were RCTs.[17] In addition most of the studies had small sample sizes. Most of the studies attracted participants who had expressed an interest in generic prescribing or who were already involved in fundholding; therefore, they have had increased motivation to save money by prescribing generic drugs which could overestimate the effects. In addition, the long term effects on generic prescribing were not reported, so it was unclear whether the observed effects were sustainable in the longer run. However, it is arguable that studies reporting benefit up to 12 months suggest that the effects can be sustained.

Implications for policy and practice

Generic prescribing in the UK NHS is already at a high level and achievement of 100% generic prescribing is neither feasible nor desirable. It is well established that thoughtless implementation of policy initiatives to replace branded drugs by generic equivalents may result in confusion for patients or in some cases actual harm.[30, 31]Indeed, the Better Care, Better Value (BCBV) indicators, introduced to support prescribing of generic proton pump inhibitors, statins and ACE inhibitors are apparently no longer published, ~~possibly reflecting concerns that they may have been used inappropriately to set targets for financial savings.~~[32]~~However, variations between areas suggest that further improvement is still possible.~~ possibly because nearly all statins and proton pump inhibitors (PPIs) are available as generics, as well as an appreciable number of angiotensin receptor blockers (ARBs).

Comment [MT1]: Comment (c)

A paper published too late for consideration for inclusion in our review outlines measures in the UK (Scotland) to encourage prescribing of generic drugs using the INN (international non-proprietary name).[33] Some European countries have systems of compulsory INN prescribing,[34] but as noted above this option has been ruled out ~~as an option~~ by the Department of Health. A further issue in Europe with limited relevance for the UK is the availability of branded generic drugs in some countries. Interventions to promote the use of these agents are similar to those for generic drugs generally, e.g. generic substitution,[35] and educational initiatives. In some healthcare systems patients may be required to meet the additional costs themselves if they are prescribed a product more expensive than the recommended (reference priced) generic drug.[36]

The main focus in the UK has been on encouraging use of generics versus patented products within a class or related class. This assumes that the products are similar in all or nearly all patients at appropriate doses, as in the drug classes covered by the BCBV indicators. There are classes of drugs for which generic forms are available but this assumption does not hold, for example atypical antipsychotics. This is because individual antipsychotic drugs differ in their adverse effect profiles and clinicians need to select the most appropriate agent based on the patient's characteristics and preferences. A recent non-systematic review found that the availability of generic risperidone in Scotland had no appreciable effect on prescribing patterns, although the authors suggested that there was potential to increase prescribing of generic atypical antipsychotics through educational activities.[37]

Evidence from a Cochrane systematic review suggests possible benefits of financial incentives to support generic prescribing.[6] The UK studies included in the review mainly relate to GP fundholding which is no longer used. Many areas use prescribing incentive schemes to support cost-effective prescribing.[29] Incentive schemes may focus on specific drugs or drug classes in accordance with local conditions.

The review of primary studies suggested that a range of interventions may be effective in increasing rates of generic prescribing. However, limitations in the evidence base make it difficult to identify any specific intervention or combination of interventions particularly suitable for implementation in the contemporary NHS setting. Decision-makers will need to consider which interventions appear most suitable to their specific setting. They may also want to consider whether the likely benefits of an intervention will outweigh its costs given the high levels of generic prescribing achieved by existing measures.

A number of systematic reviews of better quality evidence have shown modest absolute increases in desired health professional behaviours associated with interventions like audit and feedback, educational meetings and outreach and reminder systems.[13, 38] Given the relative consistency of results, this evidence in conjunction with our review findings could help in estimating the likely impact of a proposed intervention on generic prescribing behaviour.

Prescribing restrictions or removal of products from reimbursement lists to encourage generic prescribing has been used in some European countries but not in the UK. An example is switching from patented to generic statins in Norway[39] and Finland.[40] A related approach is to lift restrictions for generic forms only, as was done for angiotensin receptor blockers in some European countries when generic losartan became available.[41] However, such policies are unlikely to be applied in the UK and as whole health system policy interventions they are outside the scope of this review.

Implications for research

Although high quality RCTs would improve the evidence base, it is unclear whether such studies would be justified, as the sample size required to demonstrate a benefit over current best practice would be large and the absolute improvement would be small. However, trials of specific interventions targeted at practices or individuals with particularly low levels of generic prescribing could be considered. Such trials should evaluate interventions that have proved successful in changing other types of behaviour and are based on a robust theory of behaviour change.

Given the existence of substantial variation between areas and individual general practices, further research may be helpful to explore the reasons for this. Research could focus on specific highly prescribed drugs with generic forms available (e.g. statins) and use a qualitative or mixed methods design.

Conclusions

Although several interventions look promising, complex interventions, methodological weaknesses and conflicting results limit the validity and applicability of the findings. In particular most of the available studies were conducted with baseline rates of generic prescribing significantly lower than the NHS is currently achieving. Based on the evidence, financial incentives with educational intervention and audit/feedback looks promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

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CONTRIBUTORSHIP STATEMENT

MH designed the search strategy and performed the literature search. TMB, DC and CMcD ~~performed the literature search,~~ screened the titles and abstracts and managed the references. All 3 reviewers (TMB, DC and CMcD) screened the retrieved papers against inclusion criteria and independently performed the data extraction and quality evaluation assessment for the review. All 3 reviewers interpreted the results. All authors have approved the manuscript and given approval for it to be published.

COMPETING INTERESTS

None

DATA SHARING STATEMENT

Extra data can be accessed by e-mailing duncan.chambers@york.ac.uk

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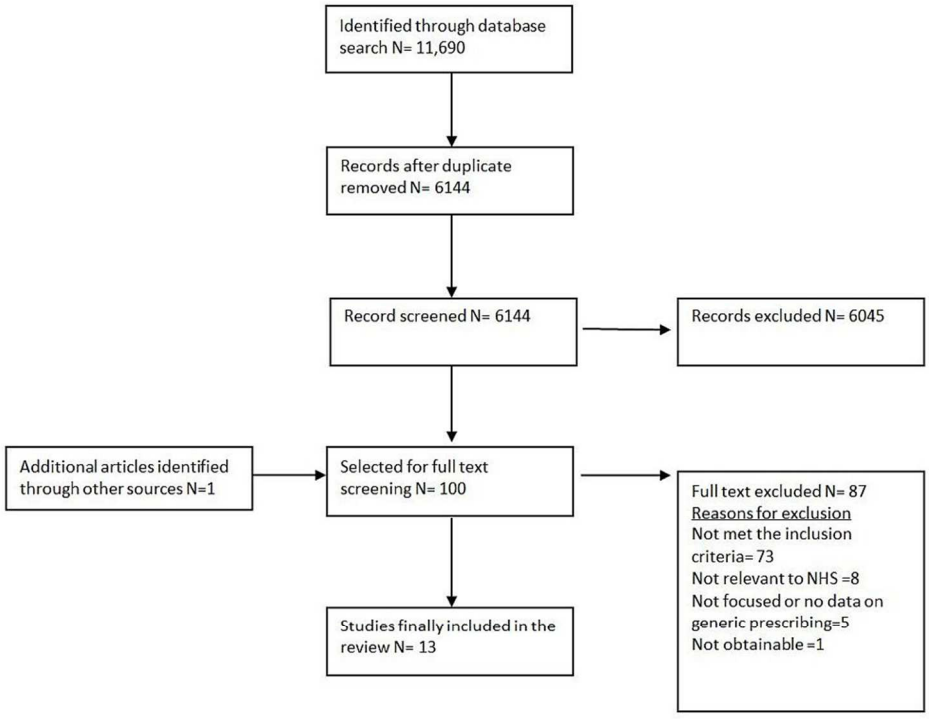

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SUPPLEMENTARY

Search strategies for the rapid review of primary literature

Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Library, Wiley

http://onlinelibrary.wiley.com/

Issue 4 of 12, April 2013

Search date: 17th May 2103

Records retrieved: 188

ID	Search	Hits
#1	MeSH descriptor: [Physician's Practice Patterns] this term only	945
#2	MeSH descriptor: [Prescriptions] this term only	70
#3	MeSH descriptor: [Drug Prescriptions] this term only	417
#4	MeSH descriptor: [Electronic Prescribing] this term only	18
#5	MeSH descriptor: [Medical Order Entry Systems] this term only	49
#6	MeSH descriptor: [Medication Systems] this term only	24
#7	MeSH descriptor: [Medication Systems, Hospital] this term only	41
#8	(prescrib* or eprescrib*):ti,ab,kw	6610
#9	(prescription* or eprescription*):ti,ab,kw	3508
#10	dispens*:ti,ab,kw	788
#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	10382
#12	MeSH descriptor: [Drugs, Generic] this term only	199
#13	generic*:ti,ab,kw	1345
#14	(non next proprietary):ti,ab,kw	7
#15	#12 or #13 or #14	1352
#16	#11 and #15	109
#17	MeSH descriptor: [Drug Substitution] this term only	58
#18	(substitut* near/2 (generic* or (non next proprietary) or therapeutic*)):ti,ab,kw	74
#19	#17 or #18	131
#20	#16 or #19 from 1985 to 2013, in Trials	188

Key:

MeSH descriptor = indexing term (MeSH heading)

* = truncation

:ti,ab,kw = terms in either title or abstract or keyword fields

near/2 = terms within two word of each other (any order)

next = terms are next to each other

CINAHL via Ebsco

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Search date: 17th May 2013

Records retrieved: 562

#	Query	Results
S24	S16 OR S22 Limiters - English Language; Published Date from: 19850101-20131231	562
S23	S16 OR S22	571
S22	S17 OR S18 OR S19 OR S20 OR S21	115
S21	TI substitut* N2 therapeutic* OR AB substitut* N2 therapeutic*	26
S20	TI substitut* N2 "non proprietary" OR AB substitut* N2 "non proprietary"	0
S19	TI substitut* N2 nonproprietary OR AB substitut* N2 nonproprietary	0
S18	TI substitut* N2 non-proprietary OR AB substitut* N2 non-proprietary	0
S17	TI substitut* N2 generic* OR AB substitut* N2 generic*	92
S16	S10 AND S15	506

S15	S11 OR S12 OR S13 OR S14	5,404
S14	TI "non proprietary" OR AB "non proprietary" OR TI non-proprietary OR AB non-proprietary	15
S13	TI nonproprietary OR AB nonproprietary	48
S12	TI generic* OR AB generic*	4,528
S11	(MH "Drugs, Generic")	1,568
S10	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9	38,541
S9	TI dispens* OR AB dispens*	2,059
S8	TI prescription* OR AB prescription* OR TI eprescription* OR AB eprescription*	12,270
S7	TI prescrib* OR AB prescrib* OR TI eprescrib* OR AB eprescrib*	18,772
S6	(MH "Practice Patterns")	3,932
S5	(MH "Medication Systems")	1,052
S4	(MH "Electronic Order Entry")	1,388
S3	(MH "Prescriptions, Drug")	3,752
S2	(MH "Prescriptive Authority")	3,771
S1	(MH "Prescribing Patterns")	1,488

Key:

MH = indexing term (CINAHL heading)

* = truncation

TI = words in the title

AB = words in the abstract

" " = phrase search

N2 = terms within two words of each other (any order)

EMBASE via OvidSP

http://ovidsp.ovid.com/

1980 to 2013 week 19

Searched on: 17th May 2013

Records retrieved: 4795

1 clinical practice/ (150206)

2 prescription/ (98358)

3 electronic prescribing/ (800)

4 computerized provider order entry/ (530)

5 (prescrib$ or eprescrib$).ti,ab. (114426)

6 (prescription$ or eprescription$).ti,ab. (75360)

7 dispens$.ti,ab. (29987)

8 or/1-7 (368968)

9 generic drug/ (7959)

10 generic$.ti,ab. (31529)

11 non-proprietary.ti,ab. (171)

12 nonproprietary.ti,ab. (234)

13 or/9-12 (35545)

14 8 and 13 (4900)

15 *drug substitution/ (335)

16 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (1055)

17 15 or 16 (1316)

18 14 or 17 (5722)

19 animal/ (1816382)

20 exp animal experiment/ (1584117)

21 Nonhuman/ (4050841)

22 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh. (4570661)

23 19 or 20 or 21 or 22 (6577334)

24 exp human/ (14329978)

25 human experiment/ (311984)

26 24 or 25 (14331371)

27 23 not (23 and 26) (5088908)

28 18 not 27 (5632)

29 limit 28 to yr="1985 -Current" (5494)

30 limit 29 to english language (4795)

Key:

/ = indexing term (EMTREE heading)

exp = exploded EMTREE heading

* = focussed EMTREE heading

$ = truncation

.ti,ab. = terms in either title or abstract fields

sh = terms in the subject heading field

adj2 = terms within two words of each other (any order)

Health Management Information Consortium via OvidSP

http://ovidsp.ovid.com/

1979 to March 2013

Searched on: 17th May 2013

Records retrieved: 228

1 exp prescribing/ (3145)

2 exp prescribing costs/ (143)

3 exp prescriptions/ (631)

4 prescription charges/ or prescription drugs/ or prescription pricing authority/ (688)

5 exp drug dispensing/ (407)

6 exp medication systems/ (37)

7 (prescrib$ or eprescrib$).ti,ab. (4632)

8 (prescription$ or eprescription$).ti,ab. (2856)

9 dispens$.ti,ab. (921)

10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (8446)

11 generic drugs/ (99)

12 generic$.ti,ab. (1263)

13 non-proprietary.ti,ab. (1)

14 nonproprietary.ti,ab. (10)

15 11 or 12 or 13 or 14 (1287)

16 10 and 15 (223)

17 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (34)

18 16 or 17 (232)

19 limit 18 to yr="1985 -Current" (228)

20 limit 19 to english (228)

Key:

/ = indexing term

exp = exploded indexing term

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

MEDLINE In-Process & Other Non-Indexed Citations and MEDLINE via OvidSP
http://ovidsp.ovid.com/

1946 to 16th May 2013

Searched on: 17th May 2013

Records retrieved: 2700

1 Physician's Practice Patterns/ (38329)

2 Prescriptions/ (1760)

3 Drug Prescriptions/ (21281)

4 Electronic Prescribing/ (451)

5 Medical Order Entry Systems/ (1318)

6 Medication Systems/ (722)

7 Medication Systems, Hospital/ (3103)

8 (prescrib$ or eprescrib$).ti,ab. (81556)

9 (prescription$ or eprescription$).ti,ab. (52201)

10 dispens$.ti,ab. (24461)

11 or/1-10 (180883)

12 Drugs, Generic/ (3329)

13 generic$.ti,ab. (26385)

14 non-proprietary.ti,ab. (125)

15 nonproprietary.ti,ab. (179)

16 or/12-15 (27814)

17 11 and 16 (2230)

18 Drug Substitution/ (665)

19 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (660)

20 17 or 18 or 19 (3233)

21 exp animals/ not humans/ (3847816)

22 20 not 21 (3206)

23 limit 22 to yr="1985 -Current" (3056)

24 limit 23 to english language (2700)

Key:

/ = indexing term (MeSH heading)

exp = exploded MeSH heading

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

PsycINFO via OvidSP

http://ovidsp.ovid.com/

1806 to May week 2 2013

Searched on: 17th May 2013

Records retrieved: 354

1 exp "prescribing (drugs)"/ (2629)

2 prescription drugs/ (2248)

3 (prescrib$ or eprescrib$).ti,ab. (19193)

4 (prescription$ or eprescription$).ti,ab. (12067)

5 dispens$.ti,ab. (2312)

6 1 or 2 or 3 or 4 or 5 (30538)

7 generic drugs/ (93)

8 generic$.ti,ab. (8365)

9 non-proprietary.ti,ab. (11)

10 nonproprietary.ti,ab. (20)

11 7 or 8 or 9 or 10 (8396)

12 6 and 11 (347)

13 (substitut$ adj2 (generic$ or non-proprietary or nonproprietary or therapeutic$)).ti,ab. (84)

14 12 or 13 (384)

15 limit 14 to yr="1985 -Current" (375)

16 limit 15 to english language (354)

Key:

/ = indexing term

exp = exploded indexing term

$ = truncation

.ti,ab. = terms in either title or abstract fields

adj2 = terms within two words of each other (any order)

PubMed

http://www.ncbi.nlm.nih.gov/pubmed

Searched on: 17th May 2013

Records retrieved: 2863

Search	Query	Items found
#56	Search #34 OR #36 OR #48 Filters: Publication date from 1985/01/01 to 2013/12/31; English Sort by: PublicationDate	2863
#53	Search #34 OR #36 OR #48 Filters: Publication date from 1985/01/01 to 2013/12/31	3222
#52	Search #34 OR #36 OR #48	3361
#48	Search (generic*[Title/Abstract]) AND substitut*[Title/Abstract]	928
#36	Search "Drug Substitution"[Mesh]	629
#34	Search #26 AND #33	2216
#33	Search #28 OR #29 OR #30	27833
#30	Search ((non-proprietary[Title/Abstract]) OR nonproprietary[Title/Abstract]) OR "non proprietary"[Title/Abstract]	296
#29	Search generic*[Title/Abstract]	26428
#28	Search "Drugs, Generic"[Mesh]	3273
#26	Search #7 OR #10 OR #13 OR #15 OR #17 OR #20 OR #22 OR #23 OR #24 OR #25	179712
#25	Search dispens*[Title/Abstract]	23786
#24	Search (prescription*[Title/Abstract]) OR eprescription*[Title/Abstract])	52177
#23	Search (prescrib*[Title/Abstract]) OR eprescrib*[Title/Abstract]	81730
#22	Search "Medication Systems, Hospital"[Mesh]	3070
#20	Search "Medication Systems"[Mesh:NoExp]	709

Search	Query	Items found
#17	Search "Medical Order Entry Systems"[Mesh]	1281
#15	Search "Electronic Prescribing"[Mesh]	431
#13	Search "Drug Prescriptions"[Mesh:NoExp]	20964
#10	Search "Prescriptions"[Mesh:NoExp]	1732
#7	Search "Physician's Practice Patterns"[Mesh]	37546

Key:

[Mesh] = exploded indexing term (MeSH heading)

[Mesh:NoExp] = indexing term (MeSH heading) not exploded

* = truncation

[Title/Abstract]) = terms in either title or abstract

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supp
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	-
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	-
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6-8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6,8,10-13
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6, 14-15
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	-
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14-15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	-
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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