Open Access Research

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

Thirimon Moe-Byrne, Duncan Chambers, Melissa Harden, Catriona McDaid

**To cite:** Moe-Byrne T, Chambers D, Harden M, *et al.* Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review. *BMJ Open* 2014;**4**:e004623. doi:10.1136/bmjopen-2013-004623

► Prepublication history and additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/bmjopen-2013-004623).

Received 5 December 2013 Revised 22 April 2014 Accepted 23 April 2014



For numbered affiliations see end of article.

Correspondence to

Duncan Chambers; duncan.chambers@york.ac.uk

#### **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 National Health Service (NHS) and similar settings.

Design: Systematic review.

**Search strategy:** We conducted a rapid evidence synthesis in two stages: First, 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. In the second stage, we searched several databases including MEDLINE and EMBASE to identify primary studies of any interventions not covered by systematic

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: 10 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 an 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 multifaceted 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 look promising but decision-makers should take into account the practicality and costs of the interventions before implementation.

## 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 general practitioner's 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 the UK National Health Service 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 substitutes for original (branded) medicines with the same quality, safety and efficacy, offer an interesting opportunity for governments and health-care payers to contain escalating healthcare budgets as their prices tend to be 10–80% lower than their proprietary equivalents. In England, the proportion of prescriptions prescribed generically (ie, by non-proprietary name rather than brand name) increased from 76% in 2002 to 83.6% in 2012.

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. A national Audit Office report in 2007 reported that prescriptions of generic statins (ie, the use of multiple sourced simvastatin and pravastatin vs patented Lipitor and Crestor) varied from 28% to 86% across English Primary Care Trusts. More recent research has also identified a marked variation in generic prescribing by general practitioners (GPs; for data on statin prescriptions in England, see http://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.<sup>4</sup> 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 National Health Service (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 a 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 the 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 the English language during the period between 1985 and May 2013 (see online supplementary 'search strategies of the rapid review of primary literature').

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 (eg, 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 to be 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 (RCTs), controlled before-and-after (CBA) studies and interrupted timeseries (ITS), based on Cochrane EPOC (Effective Practice and Organisation of Care) Group definitions, were eligible. The primary outcome was any measure of the rate of prescribing or dispensing of generic drugs (relative to the 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, and 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 1 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.<sup>6</sup> <sup>7</sup> 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.<sup>6</sup> There was evidence across all the studies included in the review of an increase in generic prescribing with fund holding, 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

Study details	Literature search end date	Summary of authors' objective	Intervention
Carroll <sup>8</sup>	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 et al <sup>11</sup>	1997	To propose effective continuing medical education strategies to improve prescribing practices	Educational strategies
Gibson et al <sup>14</sup>	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 et al <sup>12</sup>	01/2009	To determine the effects of a pharmaceutical policy restricting the reimbursement of selected medications on drug use, healthcare utilisation, health outcomes and costs	Policy restrictions on reimbursed drugs
Ivers et al <sup>13</sup>	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 <i>et al<sup>7</sup></i>	01/2012	To inquire into the nature, extent and strength of the evidence for successful implementation of progeneric medicine policies in low-income and middle-income countries	Progeneric medicine policies
Mitchell and Sullivan <sup>10</sup>	1997	To appraise findings from studies examining the impact of computers on primary care consultations	Computer systems for use by doctors during consultations
McKibbon <i>et al</i> <sup>9</sup>	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 et al 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 (fund holding, drug budgets)

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 13.6–23%). The authors reported that budgeting funds to a group of individual physicians (ie, giving them financial responsibility for their own budget) increased the use of generic drugs. However, the majority of studies had serious limitations and the authors cautioned that the results should be interpreted with care.

The second review with a strong focus on generic prescribing, which was less relevant to the UK NHS, focused on policy intervention in LMICs. The review found insufficient evidence to determine which progeneric policies increase utilisation of generic medicines in this setting. 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. Overall, most of the interventions considered in the reviews showed an increase in generic prescribing.

## 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 the 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. One study was unobtainable. 15

#### 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 a control group).  $^{27}$   $^{28}$ 

Most of the studies were in a primary care setting; five were conducted in the UK. <sup>17</sup> <sup>21–24</sup> The interventions were single or multicomponent and included professional educational interventions (two studies), physicians' collaboration with pharmacists (two studies), electronic prescribing (two studies) and multifaceted interventions, which also included the above interventions as well as networking, feedback and financial incentives (seven studies) (table 4). Most of the control groups used usual practice or no intervention. Where reported, the baseline generic prescribing rates ranged from 3.12% to 69.4% in the intervention groups and from 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.

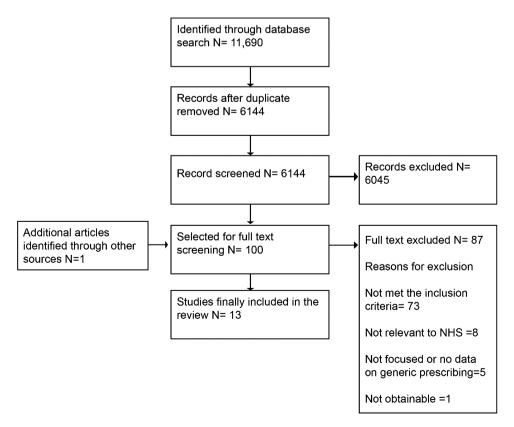


Figure 1 Study flow diagram.

Table 2 Risk of bias for RCTs and CBA studies									
	1	2	3	4	5	6	7	8	9
RCTs									
Braybrook and Walker <sup>17</sup>	UC	Н	L	Н	UC	UC	L	L	_
Meyer <i>et al</i> <sup>16</sup>	L	L	L	UC	UC	UC	L	L	Н
CBA									
Fischer <i>et al</i> <sup>20</sup>	Н	Н	L	Н	Н	L	L	L	L
Geoghegan <i>et al</i> <sup>21</sup>	Н	Н	L	UC	UC	L	L	L	UC
Leach and Wakeman <sup>22</sup>	Н	Н	L	UC	UC	L	L	L	L
Mastura and Teng <sup>19</sup>	Н	Н	Н	UC	UC	Н	L	L	Н
Niquille <i>et al</i> <sup>26</sup>	Н	Н	UC	UC	UC	Н	L	Н	_
Onion and Dutton <sup>23</sup>	Н	Н	L	UC	L	L	L	L	L
Walker and Mathers <sup>24</sup>	Н	Н	Н	Н	UC	UC	L	L	_
Wensing <i>et al</i> <sup>25</sup>	Н	Н	L	UC	L	L	L	L	Н
Wensing et al <sup>18</sup>	Н	Н	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 and (9) other risk of bias.

CBA, controlled before-and-after; H, high; L, low; RCT, randomised controlled trials; UC, unclear.

#### Narrative synthesis of intervention studies

#### **Educational interventions**

One CBA<sup>19</sup> and one RCT, 16 both had methodological limitations, evaluated an educational intervention. There was a statistically significant increase in use of generic drugs for upper respiratory tract infection at 3-month follow-up in the RCT (p<0.05). 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 with the control group, but there was a very strong imbalance at baseline (intervention: pre 33.9%, post 19%; control: pre 82%; post 88.1%). 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 GPs. 21 22 There was some baseline imbalance in one study. 22 Both studies showed

 Table 3 Risk of bias for ITS studies

 1
 2
 3
 4
 5
 6
 7

 Lopez-Picazo Ferrer et al 28
 UC
 L
 L
 L
 UC
 L
 H

 Stenner et al 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 and (7) other risk of bias.

H, high; L, low; ITS, interrupted time-series; UC, unclear.

improvement in generic prescribing rates, though in one study this was not statistically significant (p=0.338).<sup>21</sup> In the second study, there was a mean increase over baseline in total generic prescribing in the intervention group compared with the control group: 9/1000 at 3 months (p>0.05), 10/1000 at 6 months (p>0.05), 35/1000 at 12 months (p<0.01).<sup>22</sup> 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. <sup>20</sup> <sup>27</sup> 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 with control. In the ITS, the proportion of generic prescribing increased from baseline in the intervention group (pre 32% to post 50%) and also increased very slightly in the control group (pre 29% to post 31% of handwritten prescriptions). The proportion of generic prescribing was still higher in the intervention group compared with the control group 2 years postintervention (p<0.0001) and significantly increased in every specialty e-prescribing (range 11.8–62.5%).<sup>27</sup>

Similarly, the CBA study reported that the e-prescription group increased their generic prescribing from baseline compared with the control group (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.<sup>20</sup>

Study details country/setting	Populations	Intervention	Control
Cluster RCT			
Braybrook and Walker <sup>17</sup> UK/primary care	General medical practices contracted to Gwent Health Authority (September 1993–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	Duimour, bookkoovo nyusoo in the		NIo Avaining
Meyer <i>et al</i> <sup>16</sup> South Africa/primary healthcare clinics	Primary healthcare nurses in the Northern Province of South Africa (1997)	Four-day effective prescribing training workshops provided by 24 provincial trainers who had previously received a generic training-of-trainers course and a 1-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 healthcare clinics randomised (11 analysed)	No training N=12 primary healthcare clinics randomised (11 analysed)
CBA			
Fischer <i>et al</i> <sup>20</sup> USA/community-based practices	Clinicians from community-based practices from Massachusetts (2003–2005)	E-prescription with FDS); e-prescription system (pocket script) identifies preferred medications, often generic medications N=1198 clinicians (clinicians needed to write at least 1 e-priscriptions)	Unenrolled prescribers (clinicians who did not use e-prescription) N=34 453 clinicians
Geoghegan <i>et al</i> <sup>21</sup> UK/primary care	General practices in St Helens and Knowsley	Prescribing meetings (at least six meetings a year) held between local GPs and community pharmacists, with the agenda determined by GPs and pharmacists N=8 practices	Practices not participating in meetings N=50 practices
Leach and Wakeman <sup>22</sup> 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 four 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 and Teng <sup>19</sup>	Medical officers from government	Group academic detailing	No intervention
Malaysia/health clinic	health clinics in Negeri Sembilan (2004)	N=5 medical officers (1 clinic, 1848 prescriptions)	N=4 medical officers (1 clinic, 1525 prescriptions)
Niquille <i>et al</i> <sup>26</sup>	General practices in the Swiss	Quality circles (N=6 circles; 6 pharmacists and 24	No intervention (N=79 to 753 GPs each
Switzerland/primary care	Canton of Fribourg who were non-dispensing physicians (1999–2007)	GPs) Groups were moderated by specifically trained pharmacists (intervention included networking,	year since 1999)
		feedback, interdisciplinary continuing education)	

Table 4 Continued			
Study details country/setting	Populations	Intervention	Control
Onion and Dutton <sup>23</sup> UK/primary care	General practitioners (GP) in the 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 and Mathers <sup>4</sup> 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/week for a year. Intervention included practice comparison feedback, peer review meetings and prescribing recommendations	No intervention (N=9 practices; 44 GPs)
Wensing <i>et al<sup>25</sup></i> 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 <i>et al<sup>18</sup></i> Germany/primary care	Primary care physicians (GPs) from three 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) <sup>28</sup> Spain/primary care	Primary care teams from four of the six health areas of Murcia (1998–2000)	N=45 practices; 339 GPs Each individual received information about the individual, team and health district prescribing 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.	N A
Stenner <i>et al<sup>27</sup></i> USA/Vanderbilt Medical Group's outpatient clinics	Healthcare practitioners at a single 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	Handwritten prescriptions that were filled at a single VUMC outpatient pharmacy (without e-prescribing, non-Rx-Star) N=4456 randomly sampled prescriptions
N A, not applicable.			

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.

#### **Multifaceted interventions**

Seven studies examined multicomponent interventions<sup>17</sup> <sup>18</sup> <sup>23–26</sup> <sup>28</sup>: 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 the three studies had a high or unclear risk of bias for most criteria. Two were conducted in the UK.<sup>17</sup> <sup>24</sup> One study reported no significant increase in the percentage of overall generic drugs compared with the control group (p=0.17),<sup>24</sup> whereas the other two studies<sup>17</sup> <sup>26</sup> reported increases in generic prescribing in the intervention group. One CBA study reported that the generic prescribing rate of the intervention group was always higher than control for the five main classes of cardiovascular drugs for 3 years but the difference between the two groups reduced over time.<sup>26</sup> The cluster RCT study reported that active and passive feedback increased generic prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) compared with the reference group (pre and post differences in the active, passive and reference groups: 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. Both studies had a high risk of bias in randomisation and allocation concealment and an unclear risk in baseline characteristics. The 2009 study, which involved 1090 GPs, reported no significant difference in prescribing generic drugs in the control group, whereas the 2004 study, which involved 90 GPs, reported a 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.<sup>23</sup> 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 group (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 3 months.<sup>23</sup>

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.<sup>28</sup> 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 it was 17.63%; absolute improvement was 14.84% and relative improvement was 15.27%.<sup>28</sup>

## 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. 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. 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 (LMICs).

We identified 13 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 multicomponent 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 the rates of generic prescribing associated with the intervention. However, only one of these was a randomised trial <sup>17</sup> and that trial was deemed to be at a relatively high risk of bias. Similarly, two of three studies with relatively similar interventions from the UK reported positive results, though one was not statistically significant. <sup>17</sup> <sup>24</sup> One study <sup>23</sup> 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 5 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 the setting, but we recognise that the context for generic prescribing differs widely between health systems. In particular, LMICs have very different issues compared 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. <sup>17</sup> 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 fund holding; 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.<sup>30</sup> <sup>31</sup> Indeed, the Better Care, Better Value (BCBV) indicators, introduced to support prescribing of generic proton pump inhibitors (PPIs), statins and ACE inhibitors, are apparently no longer published,<sup>32</sup> possibly because nearly all statins and 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 international non-proprietary name (INN). Some European countries have systems of compulsory INN prescribing,<sup>34</sup> but as noted above this option has been ruled out by the Department of Health. A further issue in Europe with limited relevance to 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, for example, generic substitution,<sup>35</sup> 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.<sup>36</sup>

The main focus in the UK has been on encouraging the 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.<sup>37</sup>

Evidence from a Cochrane systematic review suggests possible benefits of financial incentives to support generic prescribing.<sup>6</sup> The UK studies included in the review mainly relate to GP fund holding, which is no longer used. Many areas use prescribing incentive schemes to support cost-effective prescribing.<sup>29</sup> 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 to be 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.<sup>13</sup> <sup>38</sup> 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<sup>39</sup> and Finland.<sup>40</sup> A related approach is to lift restrictions for generic forms only, as was done for ARBs in some European countries when generic losartan became available.<sup>41</sup> 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 (eg, 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 look promising, but decision-makers should take into account the practicality and costs of the interventions before implementation.

#### **Author affiliations**

<sup>1</sup>University of York, Centre for Reviews and Dissemination, York, UK <sup>2</sup>University of York, York Trials Unit, York, UK

**Acknowledgements** The authors thank Debbie Needham and Professor lan Watt for their comments on the protocol and project report, and Professor Carl Thompson for commenting on the project report.

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

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

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

**Data sharing statement** Full report (including barriers and facilitators) can be available by emailing duncan.chambers@york.ac.uk.

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/3.0/

#### **REFERENCES**

- The European Parliament and the Council of the European Union. Directive 2004/27/EC of the European Parliament and of the Council of 31st March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use. Off J Eur Union 2004;136:34–57.
- Simoens S, De Coster S. Sustaining generic medicines markets in Europe. J Generic Med 2006;3:257–68.
- Prescribing and Primary Care Services Health and Social Care Information Centre. Prescriptions dispensed in the community: England 2002–12. Health and Social Care Information Centre, 2013.
- Department of Health. The proposals to implement 'Generic Substitution' in primary care, further to the Pharmaceutical Price Regulation Scheme (PPRS) 2009: response to the consultation. London: Department of Health; 2010.
- National Audit Office. Prescribing costs in primary care. London: The Stationery Office, 2007.
- Sturm H, Austvoll-Dahlgren A, Aaserud M, et al. Pharmaceutical policies: effects of financial incentives for prescribers. Cochrane Database Syst Rev 2007;(3):CD006731.
- Kaplan WA, Ritz LS, Vitello M, et al. Policies to promote use of generic medicines in low and middle income countries: a review of published literature, 2000–2010. Health Policy 2012;106:211–24.
- Carroll NV. Do community pharmacists influence prescribing? J Am Pharm Assoc 2003;43:612–21.
- McKibbon KA, Lokker C, Handler SM, et al. Enabling medication management through health information technology. Rockville, MD: Agency for Healthcare Research and Quality, 2011.
- Mitchell E, Sullivan F. A descriptive feast but an evaluative famine: systematic review of published articles on primary care computing during 1980–97. BMJ 2001;322:279–82.

- Figueiras A, Sastre I, Gestal-Otero JJ. Effectiveness of educational interventions on the improvement of drug prescription in primary care: a critical literature review. J Eval Clin Pract 2001;7:223–41.
- Green CJ, Maclure M, Fortin PM, et al. Pharmaceutical policies: effects of restrictions on reimbursement. Cochrane Database Syst Rev 2010;(8):CD008654.
- Ivers N, Jamtvedt G, Flottorp S, et al. Audit and feedback: effects on professional practice and healthcare outcomes. Cochrane Database Syst Rev 2012;(6):CD000259.
- Gibson TB, Ozminkowski RJ, Goetzel RZ. The effects of prescription drug cost sharing: a review of the evidence. Am J Manag Care 2005;11:730–40.
- Newcastle and North Tyneside Health Authority. Precept: Prescribing cost effectiveness programme toolkit. Newcastle: Newcastle and North Tyneside Health Authority; 1999.
- Meyer JC, Summers RS, Moller H. Randomized, controlled trial of prescribing training in a South African province. *Med Educ* 2001;35:833–40.
- Braybrook S, Walker R. Influencing NSAID prescribing in primary care using different feedback strategies. *Pharm World Sci* 2000;22:39–46.
- Wensing M, Broge B, Riens B, et al. Quality circles to improve prescribing of primary care physicians. Three comparative studies. Pharmacoepidemiol Drug Saf 2009;18:763–9.
- Mastura I, Teng CL. The effect of "group detailing" on drug prescribing in primary care. *Med J Malaysia* 2008;63:315–18.
   Fischer MA, Vogeli C, Stedman M, *et al.* Effect of electronic
- Fischer MA, Vogeli C, Stedman M, et al. Effect of electronic prescribing with formulary decision support on medication use and cost. Arch Intern Med 2008;168:2433–9.
- Geoghegan M, Pilling M, Holden J, et al. A controlled evaluation of the effect of community pharmacists on general practitioner prescribing. Pharm J 1998;261:864–6.
- Leach RH, Wakeman A. An evaluation of the effectiveness of community pharmacists working with GPs to increase the cost-effectiveness of prescribing. *Pharm J* 1999;263:206–9.
- Onion CWR, Dutton C. Improving prescribing in primary care: goals, emotions, and personal agency beliefs. *Clin Manag* 1998;7:117–20.
- Walker J, Mathers N. The impact of a general practice group intervention on prescribing costs and patterns. Br J Gen Pract 2002;52:181–6.
- Wensing M, Broge B, Kaufmann-Kolle P, et al. Quality circles to improve prescribing patterns in primary medical care: what is their actual impact? J Eval Clin Pract 2004;10:457–66.
- Niquille A, Ruggli M, Buchmann M, et al. The nine-year sustained cost-containment impact of Swiss pilot physicians-pharmacists quality circles. Ann Pharmacother 2010;44:650–7.

- Stenner SP, Chen Q, Johnson KB. Impact of generic substitution decision support on electronic prescribing behavior. *JAMA* 2010:17:681–8.
- Lopez-Picazo Ferrer JJ, Sanz Moreno JA, Bernal Montanes JM, et al. Evaluating, improving and monitoring generic drug prescription. Aten Primaria 2002;29:397–406.
- Department of Health. Strategies to achieve cost-effective prescribing: guidance for Primary Care Trusts and Clinical Commissioning Groups. Leeds: Department of Health, 2010.
- Duerden MG, Hughes DA. Generic and therapeutic substitutions in the UK: are they a good thing? Br J Clin Pharmacol 2010;70:335–41.
- Ferner RE, Lenney W, Marriott JF. Controversy over generic substitution. BMJ 2010;340:c2548.
- 32. Department of Health. Cost-effective prescribing: Better Care Better Value (BCBV) indicator on statins. London: Department of Health, 2011.
- Godman B, Bishop I, Finlayson AE, et al. Reforms and initiatives in Scotland in recent years to encourage the prescribing of generic drugs, their influence and implications for other countries. Expert Rev PharmacoEconomics Outcomes Res 2013;13:469–82.
- 34. Garuoliene K, Godman B, Gulbinovic J, *et al.* European countries with small populations can obtain low prices for drugs: Lithuania as a case history. *Expert Rev PharmacoEconomics Outcomes Res* 2011;11:343–9.
- Andersson KA, Petzold MG, Allebeck P, et al. Influence of mandatory generic substitution on pharmaceutical sales patterns: a national study over five years. BMC Health Serv Res 2008;8:50.
- Dylst P, Vulto A, Simoens S. The impact of reference-pricing systems in Europe: a literature review and case studies. Expert Rev PharmacoEconomics Outcomes Res 2011;11:729–37.
- Bennie M, Bishop I, Godman B, et al. Are specific initiatives required to enhance prescribing of generic atypical antipsychotics in Scotland?: international implications. Int J Clin Pract 2013;67:170–80
- O'Brien MA, Oxman AD, Davis DA, et al. Educational outreach visits: effects on professional practice and health care outcomes. Cochrane Database Syst Rev 2007;(4):CD000409.
- Sakshaug S, Furu K, Karlstad O, et al. Switching statins in Norway after new reimbursement policy: a nationwide prescription study. Br J Clin Pharmacol 2007;64:476–81.
- Martikainen JE, Saastamoinen LK, Korhonen MJ, et al. Impact of restricted reimbursement on the use of statins in Finland: a register-based study. Med Care 2010;48:761–6.
- Bucsics A, Godman B, Burkhardt T, et al. Influence of lifting prescribing restrictions for losartan on subsequent losartan utilization patterns in Austria: implications for other countries. Expert Rev PharmacoEconomics Outcomes Res 2012;12:809–19.