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Perceptions of generic medication in the general population, doctors and

pharmacists: systematic review and meta-analysis

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ABSTRACT

Objective To investigate negative perceptions about generic medicines and evaluate the proportions of lay people, doctors and pharmacists who hold these perceptions.

Design A systematic review and meta analysis of observational studies

Data Sources Medline, Embase, PsycInfo and Scopus.

Eligibility Criteria Quantitative data from cross-sectional and prospective studies published in English after 1980 using self-report measures to evaluate perceptions about generic medicines, presented as percentages of the total sample assessed.

Results After screening 2484 articles, 42 articles were included in the final analysis. A high proportion of doctors, pharmacists and lay people had negative perceptions of generics. Lay people were significantly more likely to view generics as less effective than branded medication (31.5%, 95% CI 30.5 to 32.5%) compared to doctors (27.1%, 25.8 to 28.4%) and pharmacists (22.9%, 20.6 to 25.6%). Pharmacists (34.4%, 31.9 to 37.0%), were significantly more likely to believe generics were of inferior quality compared to branded medication than doctors (26.1%, 24.3 to 26.4%) and lay people (25.5%, 24.6 to 26.4%). Doctors believed generics caused more side effects than branded medication (24.3%, 21 to 27.9%) compared to pharmacists (17.6%, 15.3 to 20.1%) and lay people (17.7%, 16.5 to 18.9). Both doctors (28.7%, 27.1 to 30.4%) and pharmacists (28%, 23.6 to 32.9%) had significantly more safety concerns about generics than lay people (18.1%, 17.1 to 19.2%). A greater proportion of lay people felt negative about generic substitution (27.9%, 27.1 to 28.8%) compared to doctors (24.1%, 22 to 26.4%) and pharmacists (11%, 9.6 to 12.7%).

Conclusions A significant proportion of medical professionals and lay people hold negative perceptions of generic medicines. It is likely these attitudes present barriers to the wider use of generics.

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Strengths and limitations of this study

- This review is a comprehensive amalgamation of current research investigating perceptions of generic medicines amongst physicians, pharmacists, and laypeople.

- Our review used widely accepted methodology to evaluate the literature and identified that significant proportion of medical professionals and lay people hold negative perceptions of generic medicines.

- The review may have increased the risk of publication bias by only including studies that were published and available through the four databases we accessed and hand searching was not performed.

- While there are a range of studies looking at general population and doctor attitudes, there were only seven studies examining pharmacist views of generics which may have reduced the accuracy of the estimates in this group.

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Introduction

Generic medicines have been available for many years and are routinely used to treat a wide range of acute and chronic illnesses. In order to be approved for use a generic medicine must be bioequivalent to the originator product and must be the same in terms of strength, safety, and quality.[1,2] Generic formulations generally provide the same therapeutic effect as branded medicines at a much more economical price. For this reason generic drugs have been increasingly popular as a method to reduce pressure on drug budgets, and now make up an increasing percentage of dispensed drugs.

Although generic medicine use has become more widespread, there is evidence that many doctors and pharmacists hold negative views of generics and resist prescribing generic medicines. Many doctors oppose brand substitution believing generic medicines to be inferior to their branded counterparts.[3] Often these views are strongly supported by pharmaceutical companies. This has resulted in strong opposition when plans were proposed to introduce generic substitution into UK primary care[4] and controversy about using generic antiepileptic drugs[5] and generic pregabalin for pain control.[6]

A number of surveys have also shown sizable proportions of patients report negative views about generics believing them to be less effective, of lower quality, and unsuitable for treatment of major illnesses when compared to their branded equivalents.[7-10] There is also evidence that these views may be reflected in higher side effect reporting and lower adherence.[10,11] If a substantial proportion of doctors, pharmacists and the general population hold negative views of generic drugs it could represent an impediment to the widespread adoption of generic medication.

We conducted a systematic review and meta-analysis to examine the attitudes towards generic drugs held by lay people, doctors and pharmacists. We extracted from the literature the proportion of negative views about generics for the following five perceptions: drug effectiveness, drug quality, likelihood of side effects, drug safety and attitude toward generic substitution or the process of replacing a branded medication with its generic equivalent.[8]

Methods

Inclusion criteria

To be eligible for inclusion in the review, studies had to be quantitative and either cross-sectional or prospective in design. They also had to be in English, published after 1980, and use self-report measures to evaluate general perceptions about generic medicines, presented as percentages of the total sample assessed.

Data sources and searches

A systematic search of databases (Medline, Embase, PsycINFO, Scopus) was conducted on 29 March 2014 to retrieve relevant articles. A comprehensive search strategy was used, including medical subject headings (MeSH) and keywords.

Data collection

One author (SG) reviewed the titles and available abstracts for all identified citations determine relevance. Following the initial review, two of the authors (SG and MS) independently reviewed full text publications to make a final selection of included studies. A structured Excel spreadsheet was used to record relevant information and ensure uniformity of evaluation for each study. Extracted data included study characteristics including country of origin, sample type (doctor, pharmacist or lay population), sample size, and proportions of participants with negative perceptions of generic medicines. The primary outcomes of this review were the proportions of participants reporting perceptions about generic medicines in terms of generic substitution, effectiveness, quality, side effects, and safety.

Quality assessment

Two reviewers (KF and LM) independently examined the full text publications to complete a quality assessment. Raters independently categorized the articles as high, acceptable or poor quality based on an evaluation of study design, participants (N, and type), demographics, recruitment method (random or other), exclusionary criteria, method of assessing perceptions (interview, questionnaire), and question quality (clarity, appropriate response options). Consensus between the two reviewers was used to resolve any disagreement. In line with Cochrane recommendations, we chose not to use a standardised

scoring system to assess study quality. Calculating a summary score was not done so as to avoid assigning 'weights' to items on the scale which are unlikely to accurately reflect their relevance and which may change across different studies.

Statistical Analyses

From the full text of each paper, the total number of participants who took part in each study and the percentage who held negative perceptions of generic medicines across the five domains were extracted. This data was used to calculate a weighted percentage of people holding negative perceptions across the relevant studies in each domain assessed by generating a total sum of the number of participants with negative views, and calculating a percentage based on the total number of respondents in each group. Following this, modified Wald 95% Confidence Intervals were calculated for each weighted percentage value. The weighted percentages and 95% Confidence Intervals were calculated using Microsoft Excel 2010 software.

In order to compare the proportion of participants from the general population, physicians, and pharmacists who held negative views of generics in each domain (substitution, effectiveness, quality, side effects, and safety), Chi-Square tests using a Yates' correction were calculated using GraphPad QuickCalcs software (http://graphpad.com/quickcalcs/). The number of participants reporting negative views and the number reporting neutral or positive (combined) were compared between two of the groups in each analysis. Multiple analyses were conducted to compare the views of the general population and physicians, the general population and pharmacists, and physicians and pharmacists across each of the domains. As this approach required multiple comparisons, a conservative Bonferroni correction with an adjusted alpha level of $p = .0033$ (.05 /15 tests) was used.

Results

Search Results

The systematic search process identified 2484 potentially relevant publications. The initial review eliminated 2341 of these publications, including duplicates, leaving 143 articles for

full text review. Of these, 61 articles were put forward for quality assessment. During this process 19 studies were eliminated (fig 1). The publication dates for these studies ranged from 1989 through 2012 and included data from 11 countries. Additional characteristics of the studies included in the review are presented in Table 1 for the general population and Table 2 for doctors and pharmacists.

Study quality

The two raters initially made identical assessments in 38 of the 46 eligible papers, yielding a Cohen's Kappa interrater reliability of 0.69, *p*<.001, which indicates substantial agreement.[12] Subsequently, each of the 8 cases on which raters disagreed was re-evaluated. For these studies, one rater had indicated acceptable and the other either high or poor quality, but in no case was there a high-poor pairing. Discussion of rationale for the non-identical ratings was completed, and the raters came to a final agreement on each of the 8 cases. Of 46 studies, 26 were classified as high-quality (from 14 countries, with publication dates from 1987 through 2013), 16 were classified as acceptable (from 13 countries, with publication dates from 1990 through 2014), and 4 were rated as being of poor quality (from 3 countries, publication dates from 2009-2013).

Perceptions of Generic Medicines

Effectiveness

A significantly greater proportion of the general population had negative views of effectiveness of generic drugs (31.48% (95%CI [30.47, 32.51]) compared to doctors (27.07% (95%CI [25.78, 28.40]), X^2 (1) = 26.24, p < .0001) and pharmacists (22.88% (95%CI [20.35, 25.62]), X^2 (1) = 29.95, p < .0001). The percentage of pharmacists who held negative views of generic effectiveness was not significantly different from physicians, X^2 (1) = 7.04, p = .008. See Figure 2 for graphical representation of results.

Quality

At least 25% of each group reported negative perceptions about the quality of generic medications. Pharmacists reported the highest percentage of negative perceptions about the quality, 34.41% (95%CI [31.92, 36.98]), a significantly greater percentage of negative

perceptions than in either the physician sample, 26.11% (95%CI [24.28, 28.02]), X^2 (1) = 27.87, p < .0001, or the general population, 25.50% (95%CI [24.59, 26.43]), X^2 (1) = 46.96, p < .0001. Physicians and general population participants did not differ significantly from one another, X^2 (1) = 0.32, p = .57.

Safety

Both doctors (28.73% (95%CI [27.11, 30.41]) and pharmacists (28.00% (95%CI [23.61, 32.86]) held more negative perceptions about the safety of generic medicines than did the general population (18.08% (95%CI [17.05, 19.15]), X^2 (1) = 123.22 and 28.24 respectively, p < .0001 Physicians, and pharmacists did not differ from one another with regard to perceived safety of generic drugs, X^2 (1) = 0.05, p = .83.

Side effects

Physicians were the most likely to hold negative perceptions about side effects caused by generic drugs in comparison to brand name alternatives, with 24.32% (95%CI [21.04, 27.93]) endorsing these views. Physicians held significantly more negative beliefs than general population groups, 17.66% (95% CI [16.53, 18.86]), X^2 (1) = 14.85, p < .0001, and pharmacists, 17.56% (95%CI [15.31, 20.06]), X^2 (1) = 10.21, p = .001. There was not a significant difference between the proportions of members of the general population and pharmacists reporting negative perceptions about side effects of generic drugs, X^2 (1) = 0.001, p = .97.

Drug substitution

Pharmacists had the lowest rates of negative perceptions about substitution of generic drugs for their brand name alternatives, 11.04% (95%CI [9.60, 12.66]). The general population had the highest proportion of negative perceptions, 27.93% (95%CI [27.06, 28.81]), followed by physicians, 24.11% (95%CI [21.95, 26.41]). Pharmacists had significantly lower rates of negative perceptions about generic drug substitution than both the general population and doctors, X^2 (1) = 208.44 and 90.14, respectively, ps <.0001. The general population samples had slightly higher negative perceptions of drug substitution than physicians, X^2 (1) = 8.84, p = .003.

Discussion

Key findings

Our systematic review identified that a significant proportion of lay people, doctors and pharmacists hold negative perceptions of generic medicines, perceiving generics as less effective, less safe, inferior in quality, and more likely to cause side effects compared to their branded equivalents. More than a quarter of doctors and the general population believed that generic drugs are less effective and of poorer quality than branded medication. A similar proportion of doctors and pharmacists had safety concerns about generics. These findings are important as previous work has suggested that negative perceptions about generic medicines are major barriers to their acceptance and widespread usage.[13] Furthermore, these findings have important implications for clinical practice, as pharmacists and medical practitioners are in a position where they can easily transmit their expectations about the effectiveness and side effects of generic medication to the patients under their care.[14,15] Research suggests that the majority of consumers learn about generic medicines from a physician or pharmacist and this medical advice is critical to consumers' decision to take a generic medication.[7,16]

Implications

Generic medicines provide cost-effective alternatives to branded medicines that allow considerable savings to health care budgets. However, if consumers are poorly informed about their equivalence to branded medication, it is highly unlikely that generic medicines will be preferred over their branded equivalents.[17] This review has identified that a significant proportion of both health professionals and consumers have negative perceptions of generic medicines. There is clearly a need for interventions aimed at the both the general population and health professions to target misperceptions of inferior quality, safety and efficacy, as well as the reasons as to why generic medicines are cheaper than brand-name equivalents, the meaning of bioequivalence, and the testing and regulatory processes involved in approving a generic medicine for general use.[13] Currently there is a lack of research

regarding what type of intervention may be effective in improving perceptions of generic medicines.

Strengths and Limitations

This review is a comprehensive amalgamation of current research investigating perceptions of generic medicines amongst physicians, pharmacists, and laypeople. The methods used to search and evaluate the literature are widely accepted. However, it is important to note that we may have increased the risk of publication bias by only including studies that were published and available through one of the four databases we accessed and hand searching was not performed. In addition, we only reviewed studies that were published in English. While there are a range of studies looking at general population and doctor attitudes, there were only seven studies examining pharmacist views of generics and three of these had fewer than 200 participants, which may have reduced the accuracy of the estimates in this group.

Conclusions

These results suggest that there are a significant number of laypeople, doctors and pharmacists with concerns about the efficacy, safety and quality of generic medicines. The negative perceptions of doctors and pharmacists are likely to be barriers to a wider acceptance of generics, as health professionals have a strong influence on patients' decisions to take generic medicine. Further work is needed on how interventions for both medical professionals and the public can reduce negative attitudes about efficacy, safety, and side effects in order to increase the acceptability of generic prescribing and substitution.

Contributors: SC and KP designed the study. SC and MS searched the literature and extracted the data. KF and LM conducted the quality analysis, analysed and interpreted the data. SC, KF and KP drafted the manuscript. AG, MS and LM contributed to the critical revision of the manuscript. SC and KP are Guarantors.

Transparency declaration: SC and KP affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Competing Interests The authors have no competing interests to report. All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval Not required

Data sharing No additional data available

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Table 1. Selected studies assessing layperson perceptions of generic medicines

Author/Date	Country	Sample	N	Substitution	Effectiveness	Quality	Side Effects	Safety
Al-Gedadi et al., 2008[16]	Malaysia	Lay	396		38.80%	38.90%	31.20%	
Babar et al., 2010[7]	NZ	Lay	441		22.90%		34.20%	
Bertoldi et al., 2005[18]	Brazil	Lay	3,182			30%		
Bradley et al., 1998[19]	UK	Lay	2,276	43.90%				
Costa-Font et al., 2014[20]	Spain	Lay	2,244	13.20%				
Figueiras et al., 2009[21]	Portugal	Lay	819	40%				
Heikkila et al., 2011[22]	Finland	Lay	1,844		19.10%			15.50%
Himmel et al., 2005[9]	Germany	Lay	804			36.70%		
Ibrahim et al., 2012[23]	Australia	Lay	503		13%	13%	5%	15%
Iosifescu et al., 2008[24]	USA	Lay	315		15.60%		11.60%	20.10%
Keenum et al., 2012[25]	USA	Lay	172		23.30%		13.40%	
Kobayashi et al., 2011[26]	Japan	Lay	1,215	46%				
Kohli & Buller, 2013[27]	USA	Lay	160		17%	28%		9%
Lebanova et al., 2012[28]	Bulgaria	Lay	216		94%	94%		94%
Omojasola et al., 2012[29]	USA	Lay	525		6%	7%	29.60%	3%
Palagyi & Lassanova, 2008[30]	Slovakia	Lay	1,777		64%	16.70%		
Perri et al., 1990[31]	USA	Lay	326		13.50%	11.40%		6.70%
Piette et al., 2010[32]	USA	Lay	806		31.60%			28.50%
Rathe et al., 2013[33]	Denmark	Lay	2,476	14.50%				
Sansgiry & Bhosle, 2004[34]	USA	Lay	505		10.92%	7.40%	5.08%	6.08%
Shrank et al., 2009[35]	USA	Lay	1,047	26.10%			9.50%	
Sicras-Mainar & Navarro-Artieda, 2012[36]	Spain	Lay (and Physician)	203			33.20%	42.30%	
N disagreeing with each statement				**2814.16**	**2514.32**	**2192.38**	**725.5**	**940.03**
Total N sampled				**10077**	**7986**	**8597**	**4107**	**5200**
OVERALL PERCENTAGE				**27.93%**	**31.48%**	**25.50%**	**17.66%**	**18.08%**

Table 2. Selected studies assessing physician and pharmacist perceptions of generic medicines

Author/Date	Country	Sample	N	Substitution	Effectiveness	Quality	Side Effects	Safety
Andersson et al., 2006[37]	Sweden	Physicians	892	16.70%				
Bower & Burkett, 1987[38]	USA	Physicians	317	37.50%				
Brust et al., 1990[39]	USA	Physicians	145	45%				
Chua et al., 2010[40]	Malaysia	Physicians	87		33%		41.40%	52.90%
Fabiano et al., 2012[41]	Italy	Physicians	303		17.50%		17.80%	
Friedman et al., 1987[42]	USA	Physicians	245		43.20%			
Gossell-Williams, 2007[43]	Jamaica	Physicians	60	13%	60%			
Gupta, 1996[44]	USA	Physicians	100		40%			
Jamshed et al., 2012[45]	Pakistan	Physicians	206		24.30%	39.30%	26.70%	41.26%
Kersnik & Peklar, 2006[46]	Slovenia	Physicians	117		11.10%			
Shrank et al., 2011[3]	USA	Physicians	506		23.50%	50%		
Sicras-Mainar & Navarro-Artieda, 2012[36]	Spain	Physician (and Lay)	201		40.80%			
Theodorou et al., 2009[47]	Greece	Physicians	1,204		14.09%	16.83%		15.37%
	Cyprus		193		5.70%	7.25%		5.70%
Tsiantou et al., 2009[48]	Greece	Physicians	1,204		40.70%			41.90%
N disagreeing with each statement				**340.89**	**1198.21**	**550.58**	**144.95**	**831.55**
Total N sampled				**1414**	**4426**	**2109**	**596**	**2894**
OVERALL PERCENTAGE				**24.11%**	**27.07%**	**26.11%**	**24.32%**	**28.73%**
Allenet & Barry, 2003[49]	France	Pharmacists	1,000	10%				
Auta et al., 2014[50]	Nigeria	Pharmacists	154	7.10%		54.50%		
Awaisu et al., 2014[51]	Qatar	Pharmacists	108	27.70%				
Babar et al., 2011[1]	New Zealand	Pharmacists	360	10.60%	50%	65%		28%
Chong et al., 2010[52]	Australia	Pharmacists	157				13.40%	
Chong et al., 2011[53]	Malaysia	Pharmacists	219			21.40%	38.40%	
Maly et al., 2013[54]	Czech Rep	Pharmacists	615		7%	16.10%	11.20%	
N disagreeing with each statement				**179.01**	**223.05**	**463.81**	**174.01**	**100.80**
Total N sampled				**1622**	**975**	**1348**	**991**	**360**
OVERALL PERCENTAGE				**11.04%**	**22.88%**	**34.41%**	**17.56%**	**28%**

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Figure 1. Flow chart of studies assessing perceptions of generics. Numbers of records from each database

Potentially relevant records after excluding duplicates (n = 2484):

Medline (n=558) PsycINFO (n=89) Embase (n=958) Scopus (n=879)

Excluded after screening titles and abstracts (n=2341)

Potentially relevant studies identified for full text evaluation (n=61)

Studies excluded in quality assessment (n=19):

Too tightly focused (n= 3)

Did not reflect perceptions of generic medicines (n= 2)

Did not yield data in percentages (n= 6)

Reported on the same data already reported in another published study (n= 4)

Poor quality rating (n=4)

Records included in review (n=46)

Figure 2. Bar graph showing the percentage (95% Confidence Interval) of participants (general population, physicians, and pharmacists) reporting negative perceptions across the domains of effectiveness, quality, safety, side effects, and substitution.
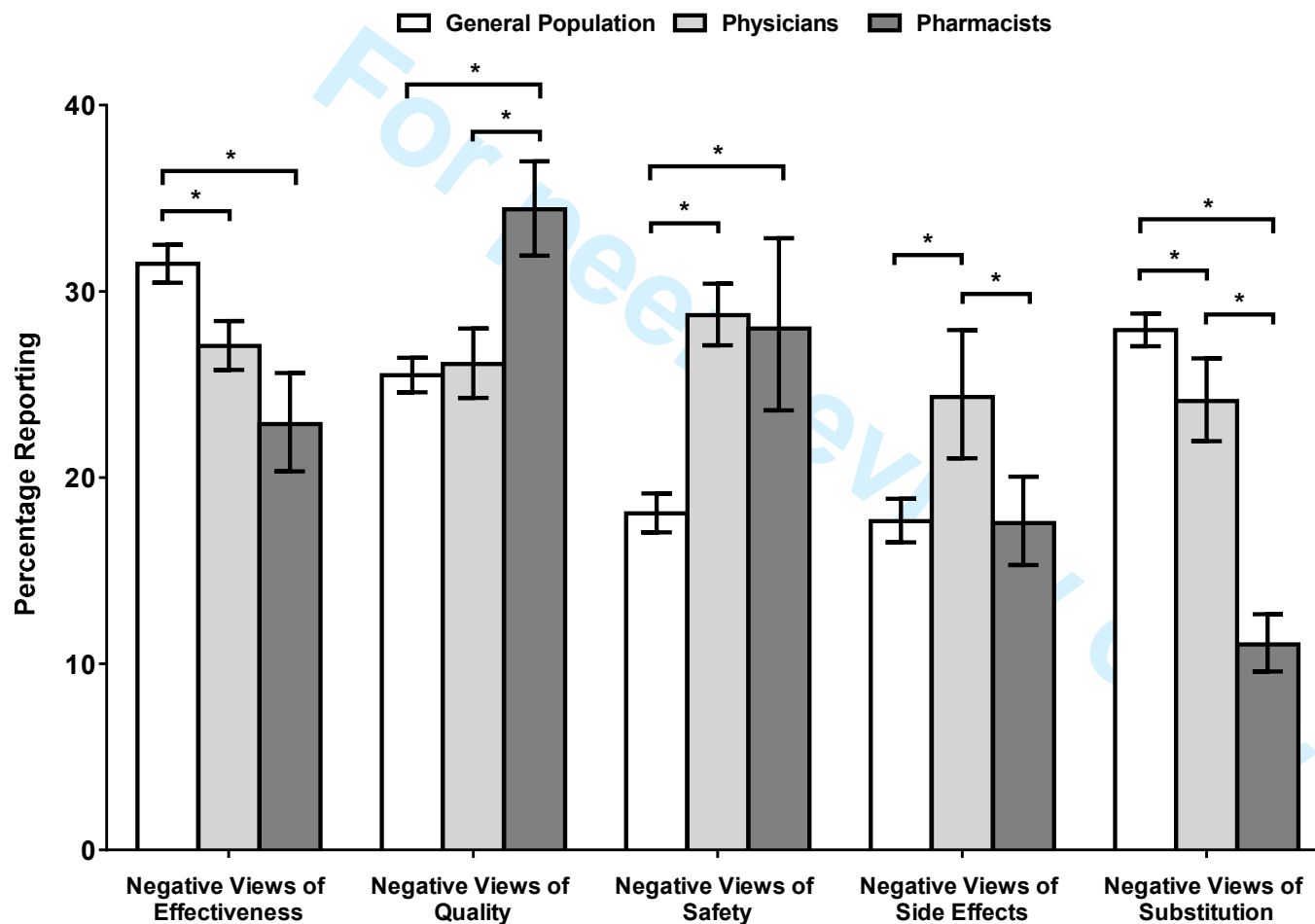
* denotes p < .0033 (Bonferroni-corrected alpha-level)

Appendix 1: Search strategies

Medline

1. MeSH terms: Drugs, Generic (exp)
2. Keyword search [title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]: (generic or nonproprietary or "non proprietary") adj3 (medic* or drug*)
3. MeSH terms: perception or perceptual distortion or social perception or attitude or "attitude of health personnel" or attitude to health or health knowledge, attitudes, practice or catastrophization or health education or consumer health information or health literacy or patient education as topic or health behavior or patient compliance or treatment refusal or illness behaviour or cross-cultural comparison or cultural characteristics or cultural diversity or social change or social class or public opinion or socioeconomic factors or patient medication knowledge or choice behaviour or drug substitution.
4. Keyword search [title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]: (perceptio* or attitud* or view* or belief* or believ* or opinion*)

Combined searches: 1 or 2 AND 3 or 4.

PsycINFO

1. MeSH terms: Generic Drugs (exp)
2. Keyword search [title, abstract, heading word, table of contents, key concepts, original title, tests & measures] : (Generic or non-proprietary or "non proprietary") adj3 (medic* or drug*)
3. MeSH terms: perception or perceptual distortion (exp) or risk perception or social perception (exp) or attitudes or adult attitudes or community attitudes or consumer attitudes (exp) or employee attitudes (exp) or female attitudes or health attitudes or health personnel attitudes (exp) or male attitudes or occupational attitudes or "physical illness (attitudes toward)" (exp) or public opinion or "racial and ethnic attitudes" (exp) or socioeconomic class attitudes (exp) or student attitudes or teacher attitudes (exp) or attitude change or attitude formation or attitude measurement or attitude measures (exp) or irrational beliefs or labeling or world view or health attitudes or health behavior or health knowledge or expectations or role expectations or cross cultural differences or cross cultural psychology or cross cultural treatment.

4. Keyword search [title, abstract, heading word, table of contents, key concepts, original title, tests & measures] : (perceptio* or attitud* or view* or belief* or believ* or opinion*).

Combined searches: 1 or 2 AND 3 or 4.

Embase

1. MeSH terms: generic drug
2. Keyword search [title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]: (generic or nonproprietary or "non proprietary") adj3 (medic* or drug*).
3. MeSH terms: nurse attitude or student attitude or physician attitude or attitude to illness or patient attitude or attitude to health or attitude or pharmacist attitude or consumer attitude or physician assistant attitude or health personnel attitude or patient education or patient preference or health education or health belief or consumer health information or health behavior or Health Belief Model or health literacy or public opinion or social environment or cultural factor.
4. Keyword search [title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]: (perceptio* or attitud* or view* or belief* or believ* or opinion*)

Combined searches: 1 or 2 AND 3 or 4.

Scopus

1. Keyword search (as title, abstract or keyword): (generic OR nonproprietary OR "non proprietary" W/3 drug* OR medic* OR pharmaceutical*) AND (perceptio* OR attitud* OR view* OR belief* OR believ* OR opinion*).

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.	No
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.	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.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
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).	7
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.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
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).	6
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.	6

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PRISMA 2009 Checklist

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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).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
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.	7 and Fig 1
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.	Table 1 and 2
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).	NA
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.	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
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).	9
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).	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
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.	11

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

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Perceptions of generic medication in the general population, doctors and pharmacists: a systematic review

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Perceptions of generic medication in the general population, doctors and

pharmacists: a systematic review

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ABSTRACT

Objective To investigate perceptions about generic medicines and evaluate the proportions of lay people, doctors and pharmacists who hold these perceptions.

Design A systematic review of observational studies.

Data Sources Medline, Embase, PsycInfo and Scopus.

Eligibility Criteria Quantitative data from cross-sectional and prospective studies published in English after 1980 using self-report measures to evaluate perceptions about generic medicines, presented as percentages of the total sample assessed.

Results After screening 2737 articles, 52 articles were included in the final analysis. A high proportion of doctors, pharmacists and lay people had negative perceptions of generics. Lay people were significantly more likely to view generics as less effective than branded medication (35.6%, 95%CI 34.8-36.4%) compared to doctors (28.7%, 27.5-29.9%) and pharmacists (23.6%, 21.2-26.2%), ps<0.0001. Pharmacists (33.4%, 31.0-35.9%) were significantly more likely to believe generics were of inferior quality compared to branded medication than doctors (28.0%, 26.3-29.9%), p=0.0006, and lay people (25.1%, 24.2-26.0%), p<0.0001. Doctors believed generics caused more side effects than branded medication (24.4%, 22.2-26.9%) compared to pharmacists (17.6%, 15.3-20.1%) and lay people (18.8%, 17.8-19.8%), ps<0.0001. Both doctors (28.5%, 26.9-30.2%) and pharmacists (25.4%, 21.4-29.9%) had significantly more safety concerns about generics than lay people (18.0%, 17.0-19.0%), ps≤0.0002. A greater proportion of lay people felt negatively about generic substitution (34.0%, 33.2-34.9%) compared to doctors (24.1%, 22.0-26.4%) and pharmacists (11.0%, 9.6-12.7%), ps<0.0001. Rates of negative perceptions of generics do not appear to have changed substantially over time in general population or physician groups, ps≥0.431, but such negative beliefs do appear to have decreased in pharmacists over the study period, p=0.034.

Conclusions A significant proportion of doctors, pharmacists and lay people hold negative perceptions of generic medicines. It is likely these attitudes present barriers to the wider use of generics.

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Strengths and limitations of this study

- This review is a comprehensive amalgamation of current research investigating perceptions of generic medicines amongst physicians, pharmacists, and laypeople.

- Our review used widely accepted methodology to evaluate the literature and identified that a significant proportion of medical professionals and lay people hold negative perceptions of generic medicines.

- The review may have increased the risk of publication bias by only including studies that were published and available through the four databases we accessed and hand searching was not performed.

- While there are a range of studies looking at general population and doctor attitudes, there were only nine studies examining pharmacist views of generics, which may have reduced the accuracy of the estimates in this group.

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Introduction

Generic medicines have been available for many years and are routinely used to treat a wide range of acute and chronic illnesses. In order to be approved for use a generic medicine must be bioequivalent to the originator product and must be the same in terms of strength, safety, and quality.[1] While generic medicines are permitted to differ from to their equivalent branded medicine in terms of colour, size, shape, and excipient ingredients, they must be able to demonstrate bioequivalence to the originator product in terms of the rate and extent of absorption.[2,3] Generic formulations provide the same therapeutic effect as branded medicines at a much more economical price. [4] For this reason generic drugs have been increasingly popular as a method to reduce pressure on drug budgets, and now make up an increasing percentage of dispensed drugs.[5]

Although generic medicine use has become more widespread, there is evidence that many doctors and pharmacists hold negative views of generics and resist prescribing generic medicines. [6,7] Many doctors oppose brand substitution believing generic medicines to be inferior to their branded counterparts.[7] Often these negative views are strongly supported by pharmaceutical companies. In France, Sanofi-Aventis was fined for disparaging generic versions of Plavix (clopidogel) and discouraging generic substitution.[8] In the UK there has been strong opposition when plans were proposed to introduce generic substitution into UK primary care[9] and controversy about using generic antiepileptic drugs[10] and generic pregabalin for pain control. [11]

A number of surveys have also shown sizable proportions of patients report negative views about generics believing them to be less effective, of lower quality, and unsuitable for treatment of major illnesses when compared to their branded equivalents.[12-15] Such negative views of generic medicines are important because they are likely to be associated with poorer health outcomes due to an association with higher side effect reporting and lower adherence.[15,16] If a substantial proportion of doctors, pharmacists and the general population hold negative views of generic drugs it could represent an impediment to the widespread adoption of generic medication.

We conducted a systematic review to examine the attitudes towards generic drugs held by lay people, doctors and pharmacists. We extracted from the literature the proportion of participants who held negative views about how generics were perceived compared to their branded equivalent for the following five perceptions: drug effectiveness, drug quality, the likelihood of causing side effects, drug safety and attitude toward generic substitution or the process of replacing a branded medication with its generic equivalent.

Methods

Inclusion criteria

To be eligible for inclusion in the review, studies had to include quantitative data presented as proportion of participants that held negative perceptions about generic medicines along any of the relevant dimensions. Studies could be either cross-sectional, mixed method or prospective in design. They also had to be in English, published in or after 1980, and use self-report measures to evaluate general perceptions about generic medicines, presented as percentages of the total sample assessed.

Data sources and searches

A systematic search of databases (Medline, Embase, PsycINFO, Scopus) was conducted on 6 September 2015 to retrieve relevant peer reviewed articles. The search strategy (Appendix 1) employed for this review drew upon common phrases and terms used in the literature concerning generic medicines and included input from a specialist librarian. Keywords (appropriately truncated to allow a wide search) were combined with medical subject headings (MeSH) to comprehensively search four databases. The strategy was modified for Scopus due to a different search platform. Hand searching was not performed, but reference lists of identified systematic reviews and narrative reviews were reviewed to identify further studies.

Data collection

One author (SC) reviewed the titles and available abstracts for all identified citations to determine relevance. Following the initial review, two of the authors (SC and MS) independently reviewed full text publications to make a final selection of included studies. A

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structured Excel spreadsheet was used to record relevant information and ensure uniformity

of evaluation for each study. Extracted data included study characteristics including country

of origin, sample type (doctor, pharmacist or lay population), sample size, and proportions of

participants with negative perceptions of generic medicines. The primary outcomes of this

review were the proportions of participants reporting perceptions about generic medicines in

terms of generic substitution, effectiveness, quality, side effects, and safety.

Quality assessment

Two reviewers (KF and LM) independently examined the full text publications to complete a

quality assessment. Raters independently categorized the articles as high, acceptable or

poor quality based on an evaluation of study design, participants (N, and type),

demographics, recruitment method (random or other), exclusionary criteria, method of

assessing perceptions (interview, questionnaire), and question quality (clarity, appropriate

response options) see Appendix 2. Consensus between the two reviewers was used to

resolve any disagreement. Studies that were classified as being of poor quality were

subsequently excluded. In line with Cochrane recommendations, we chose not to use a

standardised scoring system to assess study quality. Calculating a summary score was not

done so as to avoid assigning 'weights' to items on the scale which are unlikely to accurately

reflect their relevance and which may change across different studies. [17]

Statistical Analyses

From the full text of each paper, the total number of participants who took part in each study

and the percentage who held negative perceptions of generic medicines across the five

domains were extracted. This data was used to calculate the proportion of participants who

reported negative views of generics compared to those who reported more accurate or

positive views. These figures were summed to yield a total proportion of negative to

neutral/positive views for each of the three population samples under investigation (general

population, physician, and pharmacist) for perceptions of effectiveness, quality, side effects,

safety, and substitution of generic medicines. Within each perception, the proportion of

negative to neutral perceptions was compared across the three participant groups using Chi-

Square tests of contingency tables with a Yates' correction using GraphPad QuickCalcs software (http://graphpad.com/quickcalcs/). As this approach required multiple comparisons, a conservative Bonferroni correction with an adjusted alpha level of p = 0.0033 (0.05 /15 tests) was used.

For additional clarity and ease of interpretation in the presentation of the results, the extracted data was also used to calculate a weighted percentage (equivalent to the number of participants reporting negative views of generics out of the total number of respondents in each sample for each perception) of people holding negative perceptions across the relevant studies in each domain assessed by generating a total sum of the number of participants with negative views, and calculating a percentage based on the total number of respondents in each group. Following this, modified Wald 95% Confidence Intervals were calculated for each weighted percentage value.[18] The weighted percentages and 95% Confidence Intervals were calculated using Microsoft Excel 2010 software.

Finally, Spearman's correlations were utilised in order to assess whether there had been a systematic change in perceptions of generic medicines over time. Correlations between publication year and the percentage of participants reporting negative perceptions were conducted to assess relationships between 1) the percentage of participants holding negative perceptions (across all participants and all five domains) and publication year, 2) the percentage of negative perceptions in each domain (across all participants) and publication year, 3) the percentage of negative perceptions across all domains within each of the three participant groups. Spearman's correlations were used because publication year was not normally distributed (almost 80% of the papers were published in the last 10 years), and were carried out using SPSS version 22 software. An overall alpha level of 0.05 was employed.

Results

Search Results

The systematic search process identified 2737 potentially relevant publications. The initial review eliminated 2582 of these publications, including duplicates, leaving 155 articles for

full text review. Of these, 73 articles were put forward for quality assessment. During this process 21 studies were eliminated (fig 1). The publication dates for these studies ranged from 1987 through 2015 and included data from 27 countries. Additional characteristics of the studies included in the review are presented in Table 1 for the general population and Table 2 for doctors and pharmacists.

Study quality

The two raters initially made identical assessments in 48 of the 58 eligible papers, yielding a Cohen's Kappa interrater reliability of 0.70, *p*<.001, which indicates substantial agreement.[19] Subsequently, each of the 10 cases on which raters disagreed was re-evaluated. For these studies, one rater had indicated acceptable and the other either high or poor quality, but in no case was there a high-poor pairing. Discussion of rationale for the non-identical ratings was completed, and the raters came to a final agreement on each of the 10 cases. Of 58 studies, 29 were classified as high-quality, 23 were classified as acceptable, and 6 were rated as being of poor quality.

Perceptions of Generic Medicines

Effectiveness

A significantly greater proportion of the general population held the view that generic drugs were less effective than their brand name equivalents (5,274/14,817; 35.59% (95%CI [34.83, 36.37]) compared to doctors (1,450/5,056; 28.68% (95%CI [27.45, 29.94]), X^2 (1) = 80.22, p < 0.0001) and pharmacists (264/1,119; 23.60% (95%CI [21.20, 26.18]), X^2 (1) = 65.57, p < 0.0001). The proportion of physicians who held these negative views was significantly greater than pharmacists, X^2 (1) = 11.57, p = 0.0007. See Figure 2 for graphical representation of results.

Quality

At least 25% of each group reported the belief that the quality of generic medications is lower than that of branded drugs. Pharmacists reported the highest proportion of negative perceptions about quality (465/1,392; 33.39% (95%CI [30.96, 35.91]), a significantly greater proportion of negative perceptions than in either the physician sample (625/2,406; 28.04%

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(95%CI [26.28, 29.87]), X^2 (1) = 11.76, p = 0.0006, or the general population

(2,290/9,119;25.11% (95%CI [24.23, 26.01]), X^2 (1) = 42.51, p < 0.0001. Physicians and

general population participants did not differ significantly from one another (after applying

the Bonferroni correction), X^2 (1) = 8.47, p = 0.0036.

Safety

A greater proportion of both doctors (836/2,928, 28.54%, 95%CI [26.93, 30.20]) and

pharmacists (103/404; 25.44%, 95%CI [21.43, 29.91]) held the perception that generic

medicines were less safe to use than branded drugs than did the general population

(942/5,242; 17.97%, 95%CI [16.96, 19.04]), X^2 (1) = 122.93 and 13.59 respectively, p <

0.0001 and = 0.0002. Physicians, and pharmacists did not differ from one another with

regard to negative perceptions of safety of generic drugs, X^2 (1) = 1.49, p = 0.22.

Side effects

Physicians were the most likely to hold inaccurate perceptions that side effects are more

frequently caused by generic drugs in comparison to brand name alternatives, with one in

four (316/1,292; 24.43%, 95%CI [22.17, 26.85]) endorsing these views. Physicians held

significantly more inaccurate beliefs about side effects than general population groups

(1,054/5,618; 18.76%, 95% CI [17.76, 19.80]), X^2 (1) = 21.09, p < 0.0001, and pharmacists

(174/991; 17.56% (95%CI [15.31, 20.06]), X^2 (1) = 15.43, p < 0.0001. There was not a

significant difference between the proportions of members of the general population and

pharmacists reporting the perception that the side effects of generic drugs are higher than

branded, X^2 (1) = 0.73, p = 0.3934.

Drug substitution

Pharmacists had the lowest rates of negative perceptions about substitution of generic drugs

for their brand name alternatives (179/1,622; 11.04%, 95%CI[9.60, 12.66]). The general

population were most likely to report unfavourable attitudes towards substituting a branded

medication with its generic equivalent (3,874/11,386; 34.03% 95%CI [33.16, 34.90]) followed

by physicians (341/1,414; 24.11%, 95%CI [21.95, 26.41]). Pharmacists had significantly

lower rates of negative perceptions about generic drug substitution than both members of

the general population and doctors, X^2 (1) = 348.72 and 90.14, respectively, ps < 0.0001.

The general population samples held more negative perceptions of drug substitution than

physicians, X^2 (1) = 55.46, p < 0.0001.

Perceptions of generic medicines over time

There was not a significant overall relationship between publication year and the percentage

of participants reporting negative perceptions of generic medicines across all participant

groups and perception domains, r = -0.04, n = 115, p = 0.641. Similarly, the percentage of

negative perceptions held across the five domains did not demonstrate a significant

correlation with publication year for beliefs about effectiveness, r = -0.03, n = 37, p = 0.853,

quality, r = -0.02, n = 25, p = 0.919, safety, r = -0.20, n = 18, p = 0.424, side effects, r = 0.08,

n = 20, p = 0.742, or appropriateness of substitution, r = -0.11, n = 15, p = 0.693. Finally, the

change in the percentage of negative perceptions over time was assessed separately across

the three participant groups. There was not a significant correlation between negative

perceptions and publication year for general population samples, r = 0.10, n = 60, p = 0.431,

or physicians, r = -0.04, n = 37, p = 0.794. However, there was a significant correlation in

pharmacists' overall negative perceptions and publication year, r = -0.50, n = 18, p = 0.034,

indicating a reduction in overall reported negative perceptions in pharmacists over time.

Discussion

Key findings

Our systematic review identified that a significant proportion of lay people, doctors and

pharmacists hold negative perceptions of generic medicines, perceiving generics as less

effective, less safe, inferior in quality, and more likely to cause side effects compared to their

branded equivalents. More than a quarter of doctors and the general population believed

that generic drugs are less effective and of poorer quality than branded medication. A similar

proportion of doctors and pharmacists had safety concerns about generics. While we did not

identify any reduction in negative views of generics in doctors or lay people over the course

of the review period, there was evidence that the percentage of negative views of

pharmacists had decreased.

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These findings are important as previous work has suggested that negative perceptions about generic medicines are major barriers to their acceptance and widespread usage.[2] Furthermore, these findings have important implications for clinical practice, as pharmacists and medical practitioners are in a position where they can easily transmit their expectations about the effectiveness and side effects of generic medication to the patients under their care.[20,21] Research suggests that the majority of consumers learn about generic medicines from a physician or pharmacist and this medical advice is critical to consumers' decision to take a generic medication.[12,22]

Implications

Generic medicines provide cost-effective alternatives to branded medicines that allow considerable savings to health care budgets. However, if consumers are poorly informed about their equivalence to branded medication, it is highly unlikely that generic medicines will be preferred over their branded equivalents.[23] This review has identified that a significant proportion of both health professionals and consumers have negative perceptions of generic medicines. There is clearly a need for interventions aimed at the both the general population and health professions to target misperceptions of inferior quality, safety and efficacy, as well as the reasons as to why generic medicines are cheaper than brand-name equivalents, the meaning of bioequivalence, and the testing and regulatory processes involved in approving a generic medicine for general use.[2] Currently there is a lack of research regarding what type of intervention may be effective in improving perceptions of generic medicines.

Strengths and Limitations

This review is a comprehensive amalgamation of current research investigating perceptions of generic medicines amongst physicians, pharmacists, and laypeople. The methods used to search and evaluate the literature are widely accepted. However, it is important to note that we may have increased the risk of publication bias by only including studies that were published and available through one of the four databases we accessed and hand searching was not performed. In addition, we only reviewed studies that were published in English and

we did not include qualitative studies, as we needed to compute the proportion of participant

between physicians, pharmacists, and lay groups. While there are a range of studies looking

at general population and doctor attitudes, there were only nine studies examining

pharmacist views of generics and five of these had fewer than 200 participants, which may

have reduced the accuracy of the estimates in this group.

Conclusions

These results suggest that there are a significant number of laypeople, doctors and

pharmacists with concerns about the efficacy, safety and quality of generic medicines. The

negative perceptions of doctors and pharmacists are likely to be barriers to a wider

acceptance of generics, as health professionals have a strong influence on patients'

decisions to take generic medicine. Further work is needed on how interventions for both

medical professionals and the public can reduce negative attitudes about efficacy, safety,

and side effects in order to increase the acceptability of generic prescribing and substitution.

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Transparency declaration: SC and KP affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Ethical approval Not required

Data sharing No additional data available

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Table 1. Selected studies assessing layperson perceptions of generic medicines

Author/Date	Country	Sample	N	Substitution	Effectiveness	Quality	Side Effects	Safety
Al-Gedadi et al., 2008[22]	Malaysia	Lay	396		38.80%	38.90%	31.20%	
Babar et al., 2010[5]	NZ	Lay	441		22.90%		34.20%	
Barbosa de Lira	Brazil	Lay	278		20.9%	14.4%		
Bertoldi et al., 2005[24]	Brazil	Lay	3,182			30%		
Bradley et al., 1998[25]	UK	Lay	2,276	43.90%				
Costa-Font et al., 2014[26]	Spain	Lay	2,244	13.20%				
Dunne et al., 2014[27]	Ireland	Lay	42		18%	24%		5%
Figueiras et al., 2009[28]	Portugal	Lay	819	40%				
Heikkila et al., 2011[29]	Finland	Lay	1,844		19.10%			15.50%
Himmel et al., 2005[14]	Germany	Lay	804			36.70%		
Ibrahim et al., 2012[30]	Australia	Lay	503		13%	13%	5%	15%
Iosifescu et al., 2008[31]	USA	Lay	315		15.60%		11.60%	20.10%
Keenum et al., 2012[32]	USA	Lay	172		23.30%		13.40%	
Kobayashi et al., 2011[33]	Japan	Lay	1,215	46%				
Kohli & Buller, 2013[34]	USA	Lay	160		17%	28%		9%
Lebanova et al., 2012[35]	Bulgaria	Lay	216		94%	94%		94%
Lira et al., 2014[36]	Brazil	Lay	278		20.9%	14.4%		
Nardi et al., 2015[37]	Brazil	Lay	5,000		30.4%			
Omojasola et al., 2012[38]	USA	Lay	525		6%	7%	29.60%	3%
Palagyi & Lassanova, 2008[39]	Slovakia	Lay	1,777		64%	16.70%		
Perri et al., 1990[40]	USA	Lay	326		13.50%	11.40%		6.70%
Piette et al., 2010[41]	USA	Lay	806		31.60%			28.50%
Rathe et al., 2013[42]	Denmark	Lay	2,476	14.50%				
Sansgiry & Bhosle, 2004[43]	USA	Lay	505		10.92%	7.40%	5.08%	6.08%
Shrank et al., 2009[44]	USA	Lay	1,047	26.10%			9.50%	
Sicras-Mainar & Navarro-Artieda, 2012[45]	Spain	Lay (and Physician)	203			33.20%	42.30%	
Wong et al., 2014[46]	Malaysia	Lay	202		23.8%	23.3%	23.8%	
Yousefi et al., 2015[47]	Iran	Lay	1,309	81%	86%		21.4%	
N reporting negative perceptions				**3,874**	**5,274**	**2,290**	**1,054**	**942**
Total N sampled				**11,386**	**14,817**	**9,119**	**5,618**	**5,242**
OVERALL PERCENTAGE				**34.03%**	**35.59%**	**25.11%**	**18.76%**	**17.97%**

Table 1. Selected studies assessing layperson perceptions of generic medicines

OVERALL PERCENTAGE				**27.93%**	**31.48%**	**25.50%**	**17.66%**	**18.08%**

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Table 2. Selected studies assessing physician and pharmacist perceptions of generic medicines

Author/Date	Country	Sample	N	Substitution	Effectiveness	Quality	Side Effects	Safety
Andersson et al., 2006[48]	Sweden	Physicians	892	16.70%				
Bower & Burkett, 1987[49]	USA	Physicians	317	37.50%				
Brust et al., 1990[50]	USA	Physicians	145	45%				
Chua et al., 2010[51]	Malaysia	Physicians	87		33%		41.40%	52.90%
Dosedel et al., 2014[52]	Czech Republic	Physicians	263		39.1%	46%	37.3%	
Dunne et al., 2014[53]	Ireland	Physicians	34		11.8%	8.8%		11.8%
Fabiano et al., 2012[54]	Italy	Physicians	303		17.50%		17.80%	
Friedman et al., 1987[55]	USA	Physicians	245		43.20%			
Gossell-Williams, 2007[56]	Jamaica	Physicians	60	13%	60%			
Jamshed et al., 2012[57]	Pakistan	Physicians	206		24.30%	39.30%	26.70%	41.26%
Kersnik & Peklar, 2006[58]	Slovenia	Physicians	117		11.10%			
Kumar et al., 2015[59]	Malaysia	Physicians	263		51.7%		19.8%	
Lewek et al., 2015[60]	Poland	Physicians	170		28.8%		12.1%	
Shrank et al., 2011[7]	USA	Physicians	506		23.50%	50%		
Sicras-Mainar & Navarro-Artieda, 2012[45]	Spain	Physician (and Lay)	201		40.80%			
Theodorou et al., 2009[61]	Greece	Physicians	1,204		14.09%	16.83%		15.37%
	Cyprus		193		5.70%	7.25%		5.70%
Tsiantou et al., 2009[62]	Greece	Physicians	1,204		40.70%			41.90%
N reporting negative perceptions				**341**	**1,450**	**675**	**316**	**836**
Total N sampled				**1,414**	**5,056**	**2,406**	**1,292**	**2,928**
OVERALL PERCENTAGE				**24.11%**	**28.68%**	**28.04%**	**24.43%**	**28.54%**
Allenet & Barry, 2003[63]	France	Pharmacists	1,000	10%				
Auta et al., 2014[64]	Nigeria	Pharmacists	154	7.10%		54.50%		
Awaisu et al., 2014[65]	Qatar	Pharmacists	108	27.70%				
Babar et al., 2011[5]	New Zealand	Pharmacists	360	10.60%	50%	65%		28%
Chong et al., 2010[66]	Australia	Pharmacists	157				13.40%	
Chong et al., 2011[6]	Malaysia	Pharmacists	219			21.40%	38.40%	
Dunne et al., 2014[67]	Ireland	Pharmacists	44		2.3%	2.3%		4.5%
Gupta, 1996[68]	USA	Pharmacists	100		40%			
Maly et al., 2013[69]	Czech Rep	Pharmacists	615		7%	16.10%	11.20%	
N reporting negative perceptions				**179**	**264**	**465**	**174**	**103**
Total N sampled				**1,622**	**1,119**	**1,392**	**991**	**404**
OVERALL PERCENTAGE				**11.04%**	**23.60%**	**33.39%**	**17.56%**	**25.44%**

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Figure 1. Flow chart of studies assessing perceptions of generics. Numbers of records from each database
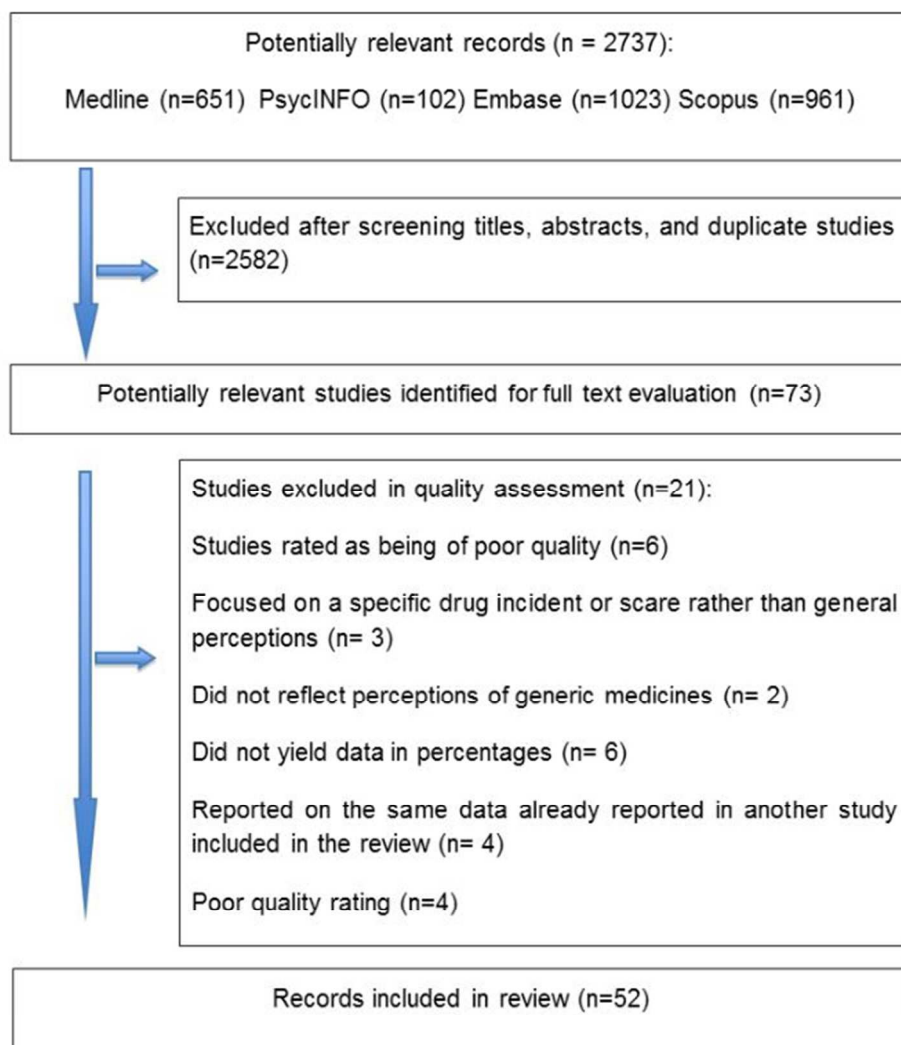
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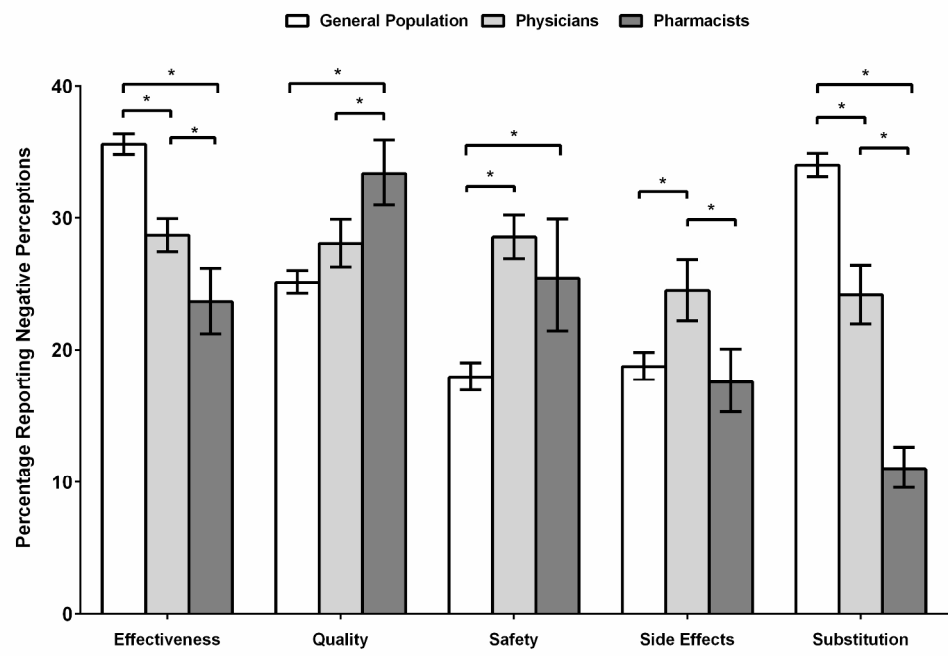31
32
33
34
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49

Potentially relevant records (n = 2737):

Medline (n=651) PsycINFO (n=102) Embase (n=1023) Scopus (n=961)

Excluded after screening titles, abstracts, and duplicate studies (n=2582)

Potentially relevant studies identified for full text evaluation (n=73)

Studies excluded in quality assessment (n=21):

Studies rated as being of poor quality (n=6)

Focused on a specific drug incident or scare rather than general perceptions (n= 3)

Did not reflect perceptions of generic medicines (n= 2)

Did not yield data in percentages (n= 6)

Reported on the same data already reported in another study included in the review (n= 4)

Poor quality rating (n=4)

Records included in review (n=52)

192x221mm (96 x 96 DPI)

255x170mm (300 x 300 DPI)

Appendix 1: Search strategies

Medline

1. MeSH terms: Drugs, Generic (exp)
2. Keyword search [title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]: (generic or nonproprietary or "non proprietary") adj3 (medic* or drug*)
3. MeSH terms: perception or perceptual distortion or social perception or attitude or "attitude of health personnel" or attitude to health or health knowledge, attitudes, practice or catastrophization or health education or consumer health information or health literacy or patient education as topic or health behavior or patient compliance or treatment refusal or illness behaviour or cross-cultural comparison or cultural characteristics or cultural diversity or social change or social class or public opinion or socioeconomic factors or patient medication knowledge or choice behaviour or drug substitution.
4. Keyword search [title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]: (perceptio* or attitud* or view* or belief* or believ* or opinion*)

Combined searches: 1 or 2 AND 3 or 4.

PsycINFO

1. MeSH terms: Generic Drugs (exp)
2. Keyword search [title, abstract, heading word, table of contents, key concepts, original title, tests & measures] : (Generic or non-proprietary or "non proprietary") adj3 (medic* or drug*)
3. MeSH terms: perception or perceptual distortion (exp) or risk perception or social perception (exp) or attitudes or adult attitudes or community attitudes or consumer attitudes (exp) or employee attitudes (exp) or female attitudes or health attitudes or health personnel attitudes (exp) or male attitudes or occupational attitudes or "physical illness (attitudes toward)" (exp) or public opinion or "racial and ethnic attitudes" (exp) or socioeconomic class attitudes (exp) or student attitudes or teacher attitudes (exp) or attitude change or attitude formation or attitude measurement or attitude measures (exp) or irrational beliefs or labeling or world view or health attitudes or health behavior or health knowledge or expectations or role expectations or cross cultural differences or cross cultural psychology or cross cultural treatment.
4. Keyword search [title, abstract, heading word, table of contents, key concepts, original title, tests & measures] : (perceptio* or attitud* or view* or belief* or believ* or opinion*).

Combined searches: 1 or 2 AND 3 or 4.

Embase

1. MeSH terms: generic drug
2. Keyword search [title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]: (generic or nonproprietary or "non proprietary") adj3 (medic* or drug*).
3. MeSH terms: nurse attitude or student attitude or physician attitude or attitude to illness or patient attitude or attitude to health or attitude or pharmacist attitude or consumer attitude or physician assistant attitude or health personnel attitude or patient education or patient preference or health education or health belief or consumer health information or health behavior or Health Belief Model or health literacy or public opinion or social environment or cultural factor.
4. Keyword search [title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]: (perceptio* or attitud* or view* or belief* or believ* or opinion*)

Combined searches: 1 or 2 AND 3 or 4.

Scopus

1. Keyword search (as title, abstract or keyword): (generic OR nonproprietary OR "non proprietary" W/3 drug* OR medic* OR pharmaceutical*) AND (perceptio* OR attitud* OR view* OR belief* OR believ* OR opinion*).

Appendix 2
Factors examined in determining quality rating

Author, date, country	
Study design	Quantitative/Qualitative:
	Type (RCT, etc.):
Major aim(s)	
Who participants are	N:
	Type (student, pharmacist, etc.):
	Demographics
	Age:
	Sex:
	Ethnicity:
	SES:
Recruitment	How recruited:
	Who excluded:
How perceptions assessed	Interview, questionnaire, archives, etc:
	Quality of questions/response options:
Which perceptions assessed	
Statistical approach (type of test/s) used	
Major finding(s)	Author main conclusions:
	% agreement, or similar:
	Effect size(s), if available:
	Additional notes:
Quality summary (study overall)	High/acceptable/poor:
	Additional notes:

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.	No
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.	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.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
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).	7
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.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
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).	6
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.	6

PRISMA 2009 Checklist

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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).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
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.	7 and Fig 1
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.	Table 1 and 2
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).	NA
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.	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
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).	9
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).	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
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.	11

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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Perceptions of generic medication in the general population, doctors and pharmacists: a systematic review

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Perceptions of generic medication in the general population, doctors and

pharmacists: a systematic review

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ABSTRACT

Objective To investigate negative perceptions about generic medicines and evaluate the proportions of lay people, doctors and pharmacists who hold these perceptions.

Design A systematic review of observational studies.

Data Sources Medline, Embase, PsycInfo and Scopus.

Eligibility Criteria Quantitative data from cross-sectional and prospective studies published in English after 1980 using self-report measures to evaluate perceptions about generic medicines, presented as percentages of the total sample assessed.

Results After screening 2737 articles, 52 articles were included in the final analysis. A high proportion of doctors, pharmacists and lay people had negative perceptions of generics. Lay people were significantly more likely to view generics as less effective than branded medication (35.6%, 95%CI 34.8-36.4%) compared to doctors (28.7%, 27.5-29.9%) and pharmacists (23.6%, 21.2-26.2%), ps<0.0001. Pharmacists (33.4%, 31.0-35.9%) were significantly more likely to believe generics were of inferior quality compared to branded medication than doctors (28.0%, 26.3-29.9%), p=0.0006, and lay people (25.1%, 24.2-26.0%), p<0.0001. Doctors believed generics caused more side effects than branded medication (24.4%, 22.2-26.9%) compared to pharmacists (17.6%, 15.3-20.1%) and lay people (18.8%, 17.8-19.8%), ps<0.0001. Both doctors (28.5%, 26.9-30.2%) and pharmacists (25.4%, 21.4-29.9%) had significantly more safety concerns about generics than lay people (18.0%, 17.0-19.0%), ps≤0.0002. A greater proportion of lay people felt negatively about generic substitution (34.0%, 33.2-34.9%) compared to doctors (24.1%, 22.0-26.4%) and pharmacists (11.0%, 9.6-12.7%), ps<0.0001. Rates of negative perceptions of generics do not appear to have changed substantially over time in general population or physician groups, ps≥0.431, *but such negative beliefs show a decreasing trend in pharmacists over the study period, p=0.034.*

Conclusions A significant proportion of doctors, pharmacists and lay people hold negative perceptions of generic medicines. It is likely these attitudes present barriers to the wider use of generics.

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Strengths and limitations of this study

- This review is a comprehensive amalgamation of current research investigating perceptions of generic medicines amongst physicians, pharmacists, and laypeople.

- Our review used widely accepted methodology to evaluate the literature and identified that a significant proportion of medical professionals and lay people hold negative perceptions of generic medicines.

- The review may have increased the risk of publication bias by only including studies that were published and available through the four databases we accessed and hand searching was not performed.

- While there are a range of studies looking at general population and doctor attitudes, there were only nine studies examining pharmacist views of generics, which may have reduced the accuracy of the estimates in this group.

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Introduction

Generic medicines have been available for many years and are routinely used to treat a wide range of acute and chronic illnesses. In order to be approved for use a generic medicine must be bioequivalent to the originator product and must be the same in terms of strength, safety, and quality.[1] While generic medicines are permitted to differ from to their equivalent branded medicine in terms of colour, size, shape, and excipient ingredients, they must be able to demonstrate bioequivalence to the originator product in terms of the rate and extent of absorption.[2,3] Generic formulations provide the same therapeutic effect as branded medicines at a much more economical price.[4] For this reason generic drugs have been increasingly popular as a method to reduce pressure on drug budgets, and now make up an increasing percentage of dispensed drugs.[5]

Although generic medicine use has become more widespread, there is evidence that many doctors and pharmacists hold negative views of generics and resist prescribing generic medicines.[6,7] Many doctors oppose brand substitution believing generic medicines to be inferior to their branded counterparts.[7] In the UK there has been strong opposition when plans were proposed to introduce generic substitution into UK primary care[8] and controversy about using generic antiepileptic drugs[9] and generic pregabalin for pain control.[10]

A number of surveys have also shown sizable proportions of patients report negative views about generics believing them to be less effective, of lower quality, and unsuitable for treatment of major illnesses when compared to their branded equivalents.[11-14] Such negative views of generic medicines are important because they are likely to be associated with poorer health outcomes due to an association with higher side effect reporting and lower adherence.[14,15] If a substantial proportion of doctors, pharmacists and the general population hold negative views of generic drugs it could represent an impediment to the widespread adoption of generic medication.

We conducted a systematic review to examine the attitudes towards generic drugs held by lay people, doctors and pharmacists. We extracted from the literature the proportion

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of participants who held negative views about how generics were perceived compared to their branded equivalent for the following five perceptions: drug effectiveness, drug quality, the likelihood of causing side effects, drug safety and attitude toward generic substitution or the process of replacing a branded medication with its generic equivalent.

Methods

Inclusion criteria

To be eligible for inclusion in the review, studies had to include quantitative data presented as proportion of participants that held perceptions about generic medicines along any of the relevant dimensions. Studies could be either cross-sectional, mixed method or prospective in design. They also had to be in English, published in or after 1980, and use self-report measures to evaluate general perceptions about generic medicines, presented as percentages of the total sample assessed.

Data sources and searches

A systematic search of databases (Medline, Embase, PsycINFO, Scopus) was conducted on 6 September 2015 to retrieve relevant peer reviewed articles. The search strategy (Appendix 1) employed for this review drew upon common phrases and terms used in the literature concerning generic medicines and included input from a specialist librarian. Keywords (appropriately truncated to allow a wide search) were combined with medical subject headings (MeSH) to comprehensively search four databases. The strategy was modified for Scopus due to a different search platform. Hand searching was not performed, but reference lists of identified systematic reviews and narrative reviews were reviewed to identify further studies.

Data collection

One author (SC) reviewed the titles and available abstracts for all identified citations to determine relevance. Following the initial review, two of the authors (SC and MS) independently reviewed full text publications to make a final selection of included studies. A structured Excel spreadsheet was used to record relevant information and ensure uniformity of evaluation for each study. Extracted data included study characteristics including country

of origin, sample type (doctor, pharmacist or lay population), sample size, and proportions of participants with negative perceptions of generic medicines. The primary outcomes of this review were the proportions of participants reporting perceptions about generic medicines in terms of generic substitution, effectiveness, quality, side effects, and safety.

Quality assessment

Two reviewers (KF and LM) independently examined the full text publications to complete a quality assessment. Raters independently categorized the articles as high, acceptable or poor quality based on an evaluation of study design, participants (N, and type), demographics, recruitment method (random or other), exclusionary criteria, method of assessing perceptions (interview, questionnaire), and question quality (clarity, appropriate response options) see Appendix 2. Consensus between the two reviewers was used to resolve any disagreement. Studies that were classified as being of poor quality were subsequently excluded. In line with Cochrane recommendations, we chose not to use a standardised scoring system to assess study quality. Calculating a summary score was not done so as to avoid assigning 'weights' to items on the scale which are unlikely to accurately reflect their relevance and which may change across different studies. [16]

Statistical Analyses

From the full text of each paper, the total number of participants who took part in each study and the percentage who held perceptions of generic medicines across the five domains were extracted. This data was used to calculate the proportion of participants who reported negative views of generics compared to those who reported more accurate or positive views. These figures were summed to yield a total proportion of negative to neutral/positive views for each of the three population samples under investigation (general population, physician, and pharmacist) for perceptions of effectiveness, quality, side effects, safety, and substitution of generic medicines. Within each perception, the proportion of negative to neutral perceptions was compared across the three participant groups using Chi-Square tests of contingency tables with a Yates' correction using GraphPad QuickCalcs software (http://graphpad.com/quickcalcs/). As this approach required multiple comparisons, a

conservative Bonferroni correction with an adjusted alpha level of p = 0.0033 (0.05 /15 tests) was used.

For additional clarity and ease of interpretation in the presentation of the results, the extracted data was also used to calculate a weighted percentage (equivalent to the number of participants reporting negative views of generics out of the total number of respondents in each sample for each perception) of people holding negative perceptions across the relevant studies in each domain assessed by generating a total sum of the number of participants with negative views, and calculating a percentage based on the total number of respondents in each group. Following this, modified Wald 95% Confidence Intervals were calculated for each weighted percentage value.[17] The weighted percentages and 95% Confidence Intervals were calculated using Microsoft Excel 2010 software.

Finally, Spearman's correlations were utilised in order to assess whether there had been a systematic change in perceptions of generic medicines over time. Correlations between publication year and the percentage of participants reporting negative perceptions were conducted to assess relationships between 1) the percentage of participants holding negative perceptions (across all participants and all five domains) and publication year, 2) the percentage of negative perceptions in each domain (across all participants) and publication year, 3) the percentage of negative perceptions across all domains within each of the three participant groups. Spearman's correlations were used because publication year was not normally distributed (almost 80% of the papers were published in the last 10 years), and were carried out using SPSS version 22 software. As this approach required multiple comparisons, a conservative Bonferroni correction with an adjusted alpha level of p = 0.0055 (0.05 /9 tests) was used.

Results

Search Results

The systematic search process identified 2737 potentially relevant publications. The initial review eliminated 2582 of these publications, including duplicates, leaving 155 articles for full text review. Of these, 73 articles were put forward for quality assessment. During this

process 21 studies were eliminated (fig 1). The publication dates for these studies ranged from 1987 through 2015 and included data from 27 countries. Additional characteristics of the studies included in the review are presented in Table 1 for the general population and Table 2 for doctors and pharmacists.

Study quality

The two raters initially made identical assessments in 48 of the 58 eligible papers, yielding a Cohen's Kappa interrater reliability of 0.70, *p*<.001, which indicates substantial agreement.[18] Subsequently, each of the 10 cases on which raters disagreed was re-evaluated. For these studies, one rater had indicated acceptable and the other either high or poor quality, but in no case was there a high-poor pairing. Discussion of rationale for the non-identical ratings was completed, and the raters came to a final agreement on each of the 10 cases. Of 58 studies, 29 were classified as high-quality, 23 were classified as acceptable, and 6 were rated as being of poor quality. The six studies rated as poor quality were removed from the analysis.

Perceptions of Generic Medicines

Effectiveness

A significantly greater proportion of the general population held the view that generic drugs were less effective than their brand name equivalents (5274/14817; 35.59% (95%CI [34.83, 36.37]) compared to doctors (1450/5056; 28.68% (95%CI [27.45, 29.94]), X^2 (1) = 80.22, p < 0.0001) and pharmacists (264/1119; 23.60% (95%CI [21.20, 26.18]), X^2 (1) = 65.57, p < 0.0001). The proportion of physicians who held these negative views was significantly greater than pharmacists, X^2 (1) = 11.57, p = 0.0007. See Figure 2 for graphical representation of results.

Quality

At least 25% of each group reported the belief that the quality of generic medications is lower than that of branded drugs. Pharmacists reported the highest proportion of negative perceptions about quality (465/1,392; 33.39% (95%CI [30.96, 35.91]), a significantly greater proportion of negative perceptions than in either the physician sample (625/2406; 28.04%

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(95%CI [26.28, 29.87]), X^2 (1) = 11.76, p = 0.0006, or the general population (2290/9119; 25.11% (95%CI [24.23, 26.01]), X^2 (1) = 42.51, p < 0.0001. Physicians and general population participants did not differ significantly from one another (after applying the Bonferroni correction), X^2 (1) = 8.47, p = 0.0036.

Safety

A greater proportion of both doctors (836/2928, 28.54%, 95%CI [26.93, 30.20]) and pharmacists (103/404; 25.44%, 95%CI [21.43, 29.91]) held the perception that generic medicines were less safe to use than branded drugs than did the general population (942/5,242; 17.97%, 95%CI [16.96, 19.04]), X^2 (1) = 122.93 and 13.59 respectively, p < 0.0001 and = 0.0002. Physicians, and pharmacists did not differ from one another with regard to negative perceptions of safety of generic drugs, X^2 (1) = 1.49, p = 0.22.

Side effects

Physicians were the most likely to hold negative beliefs that side effects are more frequently caused by generic drugs in comparison to brand name alternatives, with one in four (316/1292; 24.43%, 95%CI [22.17, 26.85]) endorsing these views. Physicians held significantly more inaccurate beliefs about side effects than general population groups (1054/5618; 18.76%, 95% CI [17.76, 19.80]), X^2 (1) = 21.09, p < 0.0001, and pharmacists (174/991; 17.56% (95%CI [15.31, 20.06]), X^2 (1) = 15.43, p < 0.0001. There was not a significant difference between the proportions of members of the general population and pharmacists reporting the perception that the side effects of generic drugs are higher than branded, X^2 (1) = 0.73, p = 0.3934.

Drug substitution

Pharmacists had the lowest rates of negative perceptions about substitution of generic drugs for their brand name alternatives (179/1622; 11.04%, 95%CI[9.60, 12.66]). The general population were most likely to report unfavourable attitudes towards substituting a branded medication with its generic equivalent (3874/11386; 34.03% 95%CI [33.16, 34.90]) followed by physicians (341/1414; 24.11%, 95%CI [21.95, 26.41]). Pharmacists had significantly lower rates of negative perceptions about generic drug substitution than both members of

the general population and doctors, X^2 (1) = 348.72 and 90.14, respectively, ps < 0.0001.

The general population samples held more negative perceptions of drug substitution than

physicians, X^2 (1) = 55.46, p < 0.0001.

Perceptions of generic medicines over time

There was not a significant overall relationship between publication year and the percentage

of participants reporting negative perceptions of generic medicines across all participant

groups and perception domains, r = -0.04, n = 115, p = 0.641. Similarly, the percentage of

negative perceptions held across the five domains did not demonstrate a significant

correlation with publication year for beliefs about effectiveness, r = -0.03, n = 37, p = 0.853,

quality, r = -0.02, n = 25, p = 0.919, safety, r = -0.20, n = 18, p = 0.424, side effects, r = 0.08,

n = 20, p = 0.742, or appropriateness of substitution, r = -0.11, n = 15, p = 0.693. Finally, the

change in the percentage of negative perceptions over time was assessed separately across

the three participant groups. There was not a significant correlation between negative

perceptions and publication year for general population samples, r = 0.10, n = 60, p = 0.431,

or physicians, r = -0.04, n = 37, p = 0.794. There was a trend (after applying the Bonferroni

correction) towards a significant correlation in pharmacists' overall negative perceptions and

publication year, r = -0.50, n = 18, p = 0.034. Although the result is not statistically

significant, it indicates a possible reduction in overall reported negative perceptions in

pharmacists over time.

Discussion

Key findings

Our systematic review identified that a significant proportion of lay people, doctors and

pharmacists hold negative perceptions of generic medicines, perceiving generics as less

effective, less safe, inferior in quality, and more likely to cause side effects compared to their

branded equivalents. More than a quarter of doctors and the general population believed

that generic drugs are less effective and of poorer quality than branded medication. A similar

proportion of doctors and pharmacists had safety concerns about generics. While we did not

identify any reduction in negative views of generics in doctors or lay people over the course

of the review period, there was some evidence that the percentage of negative views of

pharmacists had decreased.

These findings are important as previous work has suggested that negative

perceptions about generic medicines are major barriers to their acceptance and widespread

usage.[2] Furthermore, these findings have important implications for clinical practice, as

pharmacists and medical practitioners are in a position where they can easily transmit their

expectations about the effectiveness and side effects of generic medication to the patients

under their care.[19,20] Research suggests that the majority of consumers learn about generic

medicines from a physician or pharmacist and this medical advice is critical to consumers'

decision to take a generic medication.[11,21]

Implications

Generic medicines provide cost-effective alternatives to branded medicines that allow

considerable savings to health care budgets. However, if consumers are poorly informed

about their equivalence to branded medication, it is highly unlikely that generic medicines

will be preferred over their branded equivalents.[22] This review has identified that a significant

proportion of both health professionals and consumers have negative perceptions of generic

medicines. There is clearly a need for interventions aimed at the both the general population

and health professions to target misperceptions of inferior quality, safety and efficacy, as

well as the reasons as to why generic medicines are cheaper than brand-name equivalents,

the meaning of bioequivalence, and the testing and regulatory processes involved in

approving a generic medicine for general use.[2] Currently there is a lack of research

regarding what type of intervention may be effective in improving perceptions of generic

medicines.

Strengths and Limitations

This review is a comprehensive amalgamation of current research investigating perceptions

of generic medicines amongst physicians, pharmacists, and laypeople. The methods used to

search and evaluate the literature are widely accepted. However, it is important to note that

we may have increased the risk of publication bias by only including studies that were

published and available through one of the four databases we accessed and hand searching was not performed. In addition, we only reviewed studies that were published in English and we did not include qualitative studies, as we needed to compute the proportion of participant between physicians, pharmacists, and lay groups. While there are a range of studies looking at general population and doctor attitudes, there were only nine studies examining pharmacist views of generics and five of these had fewer than 200 participants, which may have reduced the accuracy of the estimates in this group.

Conclusions

These results suggest that there are a significant number of laypeople, doctors and pharmacists with concerns about the efficacy, safety and quality of generic medicines. The negative perceptions of doctors and pharmacists are likely to be barriers to a wider acceptance of generics, as health professionals have a strong influence on patients' decisions to take generic medicine. Further work is needed on how interventions for both medical professionals and the public can reduce negative attitudes about efficacy, safety, and side effects in order to increase the acceptability of generic prescribing and substitution.

Data sharing No additional data available

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Table 1. Selected studies assessing layperson perceptions of generic medicines

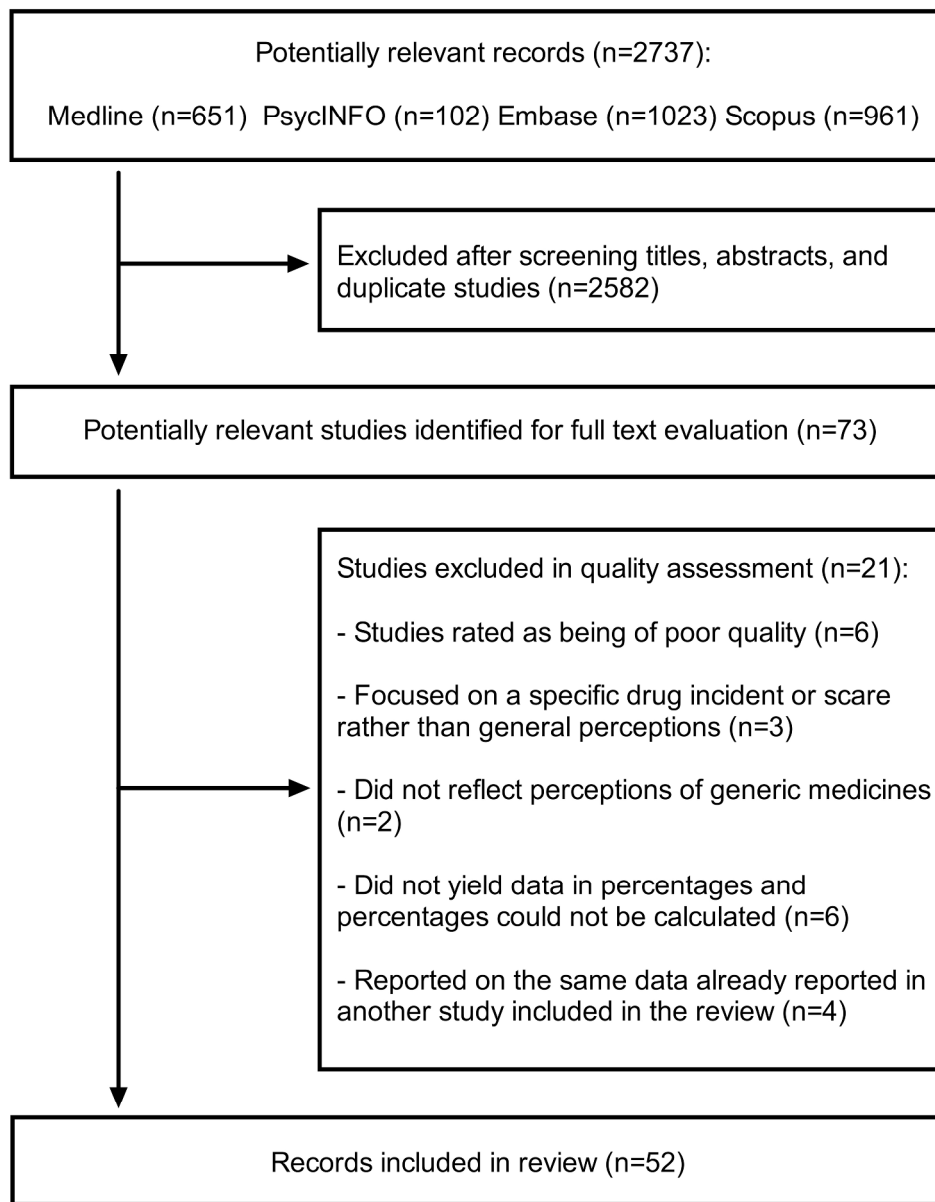| Author/Date	Country	Sample	N	Substitution	Effectiveness	Quality	Side Effects	Safety
Al-Gedadi et al., 2008[21]	Malaysia	Lay	396		38.80%	38.90%	31.20%	
Babar et al., 2010[5]	NZ	Lay	441		22.90%		34.20%	
Bertoldi et al., 2005[23]	Brazil	Lay	3,182			30%		
Bradley et al., 1998[24]	UK	Lay	2,276	43.90%				
Costa-Font et al., 2014[25]	Spain	Lay	2,244	13.20%				
Dunne et al., 2014[26]	Ireland	Lay	42		18%	24%		5%
Figueiras et al., 2009[27]	Portugal	Lay	819	40%				
Heikkila et al., 2011[28]	Finland	Lay	1,844		19.10%			15.50%
Himmel et al., 2005[13]	Germany	Lay	804			36.70%		
Ibrahim et al., 2012[29]	Australia	Lay	503		13%	13%	5%	15%
Iosifescu et al., 2008[30]	USA	Lay	315		15.60%		11.60%	20.10%
Keenum et al., 2012[31]	USA	Lay	172		23.30%		13.40%	
Kobayashi et al., 2011[32]	Japan	Lay	1,215	46%				
Kohli & Buller, 2013[33]	USA	Lay	160		17%	28%		9%
Lebanova et al., 2012[34]	Bulgaria	Lay	216		94%	94%		94%
Lira et al., 2014[35]	Brazil	Lay	278		20.9%	14.4%		
Nardi et al., 2015[36]	Brazil	Lay	5,000		30.4%			
Omojasola et al., 2012[37]	USA	Lay	525		6%	7%	29.60%	3%
Palagyi & Lassanova, 2008[38]	Slovakia	Lay	1,777		64%	16.70%		
Perri et al., 1990[39]	USA	Lay	326		13.50%	11.40%		6.70%
Piette et al., 2010[40]	USA	Lay	806		31.60%			28.50%
Rathe et al., 2013[41]	Denmark	Lay	2,476	14.50%				
Sansgiry & Bhosle, 2004[42]	USA	Lay	505		10.92%	7.40%	5.08%	6.08%
Shrank et al., 2009[43]	USA	Lay	1,047	26.10%			9.50%	
Sicras-Mainar & Navarro-Artieda, 2012[44]	Spain	Lay (and Physician)	203			33.20%	42.30%	
Wong et al., 2014[45]	Malaysia	Lay	202		23.8%	23.3%	23.8%	
Yousefi et al., 2015[46]	Iran	Lay	1,309	81%	86%		21.4%	
N reporting negative perceptions				**3,874**	**5,274**	**2,290**	**1,054**	**942**
Total N sampled				**11,386**	**14,817**	**9,119**	**5,618**	**5,242**
OVERALL PERCENTAGE				**34.03%**	**35.59%**	**25.11%**	**18.76%**	**17.97%**

Table 2. Selected studies assessing physician and pharmacist perceptions of generic medicines

Author/Date	Country	Sample	N	Substitution	Effectiveness	Quality	Side Effects	Safety
Andersson et al., 2006[47]	Sweden	Physicians	892	16.70%				
Bower & Burkett, 1987[48]	USA	Physicians	317	37.50%				
Brust et al., 1990[49]	USA	Physicians	145	45%				
Chua et al., 2010[50]	Malaysia	Physicians	87		33%		41.40%	52.90%
Dosedel et al., 2014[51]	Czech Republic	Physicians	263		39.1%	46%	37.3%	
Dunne et al., 2014[52]	Ireland	Physicians	34		11.8%	8.8%		11.8%
Fabiano et al., 2012[53]	Italy	Physicians	303		17.50%		17.80%	
Friedman et al., 1987[54]	USA	Physicians	245		43.20%			
Gossell-Williams, 2007[55]	Jamaica	Physicians	60	13%	60%			
Jamshed et al., 2012[56]	Pakistan	Physicians	206		24.30%	39.30%	26.70%	41.26%
Kersnik & Peklar, 2006[57]	Slovenia	Physicians	117		11.10%			
Kumar et al., 2015[58]	Malaysia	Physicians	263		51.7%		19.8%	
Lewek et al., 2015[59]	Poland	Physicians	170		28.8%		12.1%	
Shrank et al., 2011[7]	USA	Physicians	506		23.50%	50%		
Sicras-Mainar & Navarro-Artieda, 2012[44]	Spain	Physician (and Lay)	201		40.80%			
Theodorou et al., 2009[60]	Greece	Physicians	1,204		14.09%	16.83%		15.37%
	Cyprus		193		5.70%	7.25%		5.70%
Tsiantou et al., 2009[61]	Greece	Physicians	1,204		40.70%			41.90%
N reporting negative perceptions				**341**	**1,450**	**675**	**316**	**836**
Total N sampled				**1,414**	**5,056**	**2,406**	**1,292**	**2,928**
OVERALL PERCENTAGE				**24.11%**	**28.68%**	**28.04%**	**24.43%**	**28.54%**
Allenet & Barry, 2003[62]	France	Pharmacists	1,000	10%				
Auta et al., 2014[63]	Nigeria	Pharmacists	154	7.10%		54.50%		
Awaisu et al., 2014[64]	Qatar	Pharmacists	108	27.70%				
Babar et al., 2011[5]	New Zealand	Pharmacists	360	10.60%	50%	65%		28%
Chong et al., 2010[65]	Australia	Pharmacists	157				13.40%	
Chong et al., 2011[6]	Malaysia	Pharmacists	219			21.40%	38.40%	
Dunne et al., 2014[66]	Ireland	Pharmacists	44		2.3%	2.3%		4.5%
Gupta, 1996[67]	USA	Pharmacists	100		40%			
Maly et al., 2013[68]	Czech Rep	Pharmacists	615		7%	16.10%	11.20%	
N reporting negative perceptions				**179**	**264**	**465**	**174**	**103**
Total N sampled				**1,622**	**1,119**	**1,392**	**991**	**404**
OVERALL PERCENTAGE				**11.04%**	**23.60%**	**33.39%**	**17.56%**	**25.44%**

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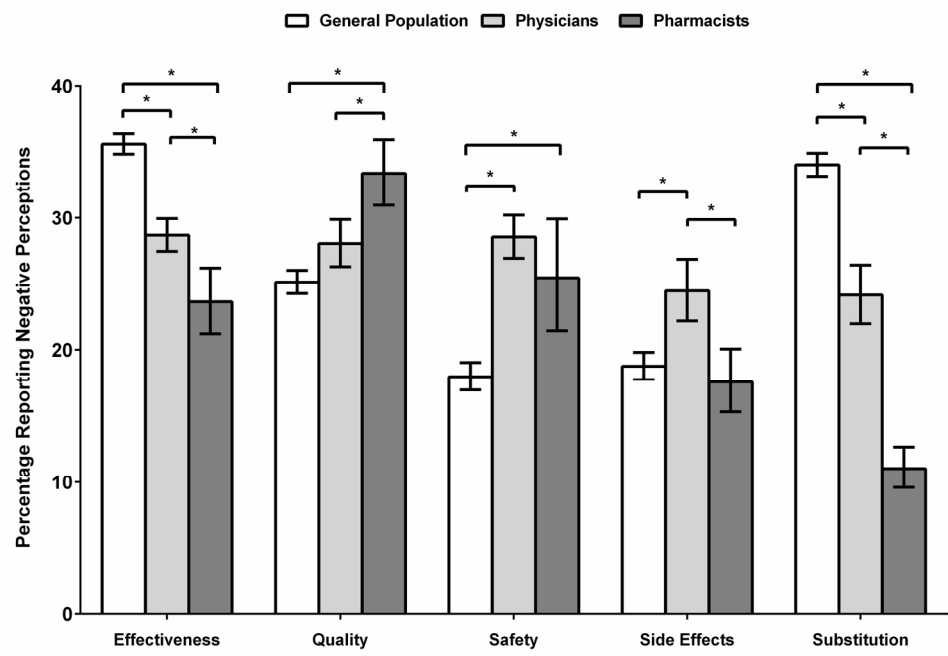Potentially relevant records (n=2737):

Medline (n=651) PsycINFO (n=102) Embase (n=1023) Scopus (n=961)

Excluded after screening titles, abstracts, and duplicate studies (n=2582)

Potentially relevant studies identified for full text evaluation (n=73)

Studies excluded in quality assessment (n=21):

- Studies rated as being of poor quality (n=6)

- Focused on a specific drug incident or scare rather than general perceptions (n=3)

- Did not reflect perceptions of generic medicines (n=2)

- Did not yield data in percentages and percentages could not be calculated (n=6)

- Reported on the same data already reported in another study included in the review (n=4)

Records included in review (n=52)

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Appendix 1: Search strategies

Medline

1. MeSH terms: Drugs, Generic (exp)
2. Keyword search [title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]: (generic or nonproprietary or "non proprietary") adj3 (medic* or drug*)
3. MeSH terms: perception or perceptual distortion or social perception or attitude or "attitude of health personnel" or attitude to health or health knowledge, attitudes, practice or catastrophization or health education or consumer health information or health literacy or patient education as topic or health behavior or patient compliance or treatment refusal or illness behaviour or cross-cultural comparison or cultural characteristics or cultural diversity or social change or social class or public opinion or socioeconomic factors or patient medication knowledge or choice behaviour or drug substitution.
4. Keyword search [title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]: (perceptio* or attitud* or view* or belief* or believ* or opinion*)

Combined searches: 1 or 2 AND 3 or 4.

PsycINFO

1. MeSH terms: Generic Drugs (exp)
2. Keyword search [title, abstract, heading word, table of contents, key concepts, original title, tests & measures] : (Generic or non-proprietary or "non proprietary") adj3 (medic* or drug*)
3. MeSH terms: perception or perceptual distortion (exp) or risk perception or social perception (exp) or attitudes or adult attitudes or community attitudes or consumer attitudes (exp) or employee attitudes (exp) or female attitudes or health attitudes or health personnel attitudes (exp) or male attitudes or occupational attitudes or "physical illness (attitudes toward)" (exp) or public opinion or "racial and ethnic attitudes" (exp) or socioeconomic class attitudes (exp) or student attitudes or teacher attitudes (exp) or attitude change or attitude formation or attitude measurement or attitude measures (exp) or irrational beliefs or labeling or world view or health attitudes or health behavior or health knowledge or expectations or role expectations or cross cultural differences or cross cultural psychology or cross cultural treatment.
4. Keyword search [title, abstract, heading word, table of contents, key concepts, original title, tests & measures] : (perceptio* or attitud* or view* or belief* or believ* or opinion*).

Combined searches: 1 or 2 AND 3 or 4.

Embase

1. MeSH terms: generic drug
2. Keyword search [title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]: (generic or nonproprietary or "non proprietary") adj3 (medic* or drug*).
3. MeSH terms: nurse attitude or student attitude or physician attitude or attitude to illness or patient attitude or attitude to health or attitude or pharmacist attitude or consumer attitude or physician assistant attitude or health personnel attitude or patient education or patient preference or health education or health belief or consumer health information or health behavior or Health Belief Model or health literacy or public opinion or social environment or cultural factor.
4. Keyword search [title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]: (perceptio* or attitud* or view* or belief* or believ* or opinion*)

Combined searches: 1 or 2 AND 3 or 4.

Scopus

1. Keyword search (as title, abstract or keyword): (generic OR nonproprietary OR "non proprietary" W/3 drug* OR medic* OR pharmaceutical*) AND (perceptio* OR attitud* OR view* OR belief* OR believ* OR opinion*).

Appendix 2
Factors examined in determining quality rating

Author, date, country	
Study design	Quantitative/Qualitative:
	Type (RCT, etc.):
Major aim(s)	
Who participants are	N:
	Type (student, pharmacist, etc.):
	Demographics
	Age:
	Sex:
	Ethnicity:
	SES:
Recruitment	How recruited:
	Who excluded:
How perceptions assessed	Interview, questionnaire, archives, etc:
	Quality of questions/response options:
Which perceptions assessed	
Statistical approach (type of test/s) used	
Major finding(s)	Author main conclusions:
	% agreement, or similar:
	Effect size(s), if available:
	Additional notes:
Quality summary (study overall)	High/acceptable/poor:
	Additional notes: