A systematic review examining the effectiveness of medicines information services for patients and the general public

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Authors’ contributions
The study was designed by MW and MJ, with advice from AJ and JS. MW was involved in all stages of the systematic review process, and drafted the manuscript. MJ, AJ and JS were involved in the screening of titles and abstracts. MJ was involved in discussions regarding the inclusion of studies and the quality assessment of studies. All authors read, provided feedback and approved the final manuscript.

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Abstract

Objectives: Hospital-based patient medicines helpline services (PMHS) and medicines information services for the general public (MISGP) are available in many countries to support people with their medicines. Our aim was to examine the available evidence regarding the effectiveness of PMHS and MISGP.

Methods: Searches were conducted using Medline, EMBASE, CINAHL, Scopus, and Web of Science, on 11th August 2018. Forward and backward citation searches were conducted, grey literature was searched, and study quality/risk of bias was assessed. Findings were synthesised in a narrative synthesis. Where appropriate, weighted means were calculated.

Key findings: Thirty-two studies were identified for inclusion (seventeen published articles, fifteen conference abstracts). Eighteen studies were conducted within the United Kingdom. Mean quality assessment was moderate (51%); risk of bias was high (63%). PMHS and MISGP are both typically perceived as positive (e.g., 94% and 91% of participants were satisfied with using a PMHS and MISGP, respectively). For PMHS, advice is reported to be usually followed (94%, and 66% for MISGP). For both services, users report several positive outcomes (e.g., problems resolved/avoided, feeling reassured, and improved health). PMHS may also be effective for correcting medicines-related errors (up to 39% of calls may concern errors), and for potentially avoiding medicines-related harm (48% of enquiries concerned situations that were judged to have the potential to harm patients).

Conclusions: Findings suggest that both PMHS and MISGP may be a beneficial source of medicines-related support. However, the moderate quality and high risk of bias of studies highlight that more high-quality research is needed.

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Keywords: systematic review, patient medicines helpline, medicines information, drug information, hospital pharmacy, drug information center.
INTRODUCTION

Prescription and over-the-counter medications are both fundamental and commonplace components of healthcare worldwide. For example, approximately half of people in both the United Kingdom and the United States of America take at least one prescribed medication on a regular basis [1, 2]. Additionally, the use of medications is increasing. In the UK, there was a 65% increase in the annual number of prescriptions dispensed between 1999 and 2009, from approximately 653 million to 1,074 million [3, 4]. A growing number of studies suggest that patients have a need for information and support regarding their medicines. Approximately 40% of patients who have been discharged from hospital may subsequently experience medicines-related problems, including medicines-related errors [5-13]. Findings indicate that patients often lack knowledge about their medications following hospital discharge [14-18], and that many patients report not receiving important medicines-related information [19-21]. World Health Organisation (WHO) policy states that offering information on medicines via Medicines Information centres, and providing public education about medicines, are two of twelve essential interventions to promote the rational use of medicines [22]. Therefore, medicines information (MI) services have been established in many countries to support patients and the general public with their medicines.

Patient medicines helpline services

In the UK, patient medicines helpline services (PMHS) are available for patients who have received care within some secondary healthcare settings [23]. The primary function of a PMHS is to enable discharged patients to communicate with a pharmacy professional from the healthcare setting where they recently received care. PMHS are therefore a means of providing medicines-related support following hospital discharge. The first PMHS was established in the UK in 1992 [24], and a survey conducted in 2017 found that 52% of NHS Trusts in England currently provide a PMHS [23].
Although PMHS were initially set up to improve patients’ knowledge and use of their medicines, recent guidelines for their implementation have suggested other benefits, for both service users and healthcare organisations [25]. Additional benefits include reducing harm to patients, highlighting and correcting medicine-related errors, reducing unnecessary use of other healthcare services, and improving the patient experience of healthcare services. While useful, the list of proposed benefits is not currently evidence-based, which is likely to limit their impact.

**Medicines Information services for the general public**

In many countries, medicines information (MI) services are provided for the general public, rather than primarily for patients of a specific hospital (from here, MI services for the general public will be referred to as MISGP). Therefore, MISGP are available for patients and also the wider community, and their aim is typically to provide information and support for any medication. Their remit therefore differs to that of PMHS, which specifically function to provide information and support regarding medication pertaining to a recent period of hospital care. MISGP are often provided from Drug Information (DI) Centres or Drug and Poison Information Centres that are often regional or national in scope rather than local to specific hospitals [26-32]. Additionally, the general public in some non-UK countries such as the United States may also have the option of acquiring MI from services that provide alternative communication methods to telephone helplines, such as online “Ask-the-Pharmacist” services [33-35].

**Aim**

To date, a review of the literature has not been conducted which brings together the available evidence as to the effectiveness of either PMHS or MISGP, nor the quality of the evidence.

The aim of this systematic review was to answer the following research question: *What is the available evidence regarding the effectiveness of PMHS and MISGP?*

**METHODS**
The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [36] was used in the planning, conducting, and reporting of this systematic review. The PRISMA statement protocol counterpart (PRISMA-P; [37]) was used to develop the protocol for this review. The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 10th October 2017 (registration number CRD42017075165) [38].

Eligibility criteria

Studies were included in this systematic review if they used any design in order to examine any outcomes for service users, service providers, and/or healthcare organisations pertaining to the effectiveness of PMHS and/or MISGP. Service users’ perceptions of the value of MI services was included as a type of effectiveness, since UK policies emphasise the importance of the patient experience, that the NHS is committed to patient involvement in healthcare, and that services should be shaped around patients’ needs [39-41].

For the purpose of this systematic review, PMHS and a MISGP were considered to have the following characteristics:

1. A service involving any type of distance communication between the service user and service provider, instigated by the service user.

2. A service primarily providing MI, and not general clinical information and advice. The service could cater for enquiries about prescribed medicines and/or over-the-counter medicines. However, services that functioned to predominantly answer enquiries about the following were excluded: complementary and alternative medicines, illicit drugs, and poisonings. Additionally, telepharmacy and e-pharmacy services typically provide a general pharmacy service rather than an MI service, albeit remotely [42]. Therefore, we excluded studies that examined telepharmacy services and/or e-pharmacy services. Services that provide MI for both healthcare professionals and patients/public...
were also considered. However, studies were only included if relevant findings for patients/public were separately reported to the findings for healthcare professionals.

(3) A service that operated from any setting, within any country.

(4) A service available over a sustained period of time. Therefore, we excluded studies that examined services that were available for a limited time only (e.g., a medicine phone-in day).

(5) For PMHS: a service for patients and/or carers of patients who received care from the healthcare organisation that provides the helpline. For MISGP: a service for the general public of a region or nation.

We included published studies (including published theses), unpublished studies, abstracts, and conference proceedings that were written in English. Abstracts and conference proceedings were only included if there was sufficient reporting of method and results to meet our study objectives. We included articles written in non-English languages where the abstract was reported in the English language, if the abstract alone provided information to support our research objectives.

We excluded studies if the data were presented in a subsequently published format (e.g., we excluded a study in a conference proceeding if it was subsequently published as a full-text article).

No restriction was made regarding year of publication.

Search strategy

Searches were conducted using Medline, EMBASE, CINAHL, Scopus, and Web of Science (Science Citation Index Expanded, Social Science Citation Index, Conference Proceedings Citation Index – Science, Conference Proceedings Citation Index – Social Science & Humanities, Emerging Sources Citation Index). Where possible, searches were conducted using both free-text and subject headings. Search terms and the search strategy were determined for EMBASE, and subsequently adapted to the syntax and subject headings of the other databases (see Supplementary file 1 for the EMBASE search strategy). Searches were conducted on 1st August 2017 and updated on 11th August.
2018. Forward and backward citation searches were conducted for all included studies. Forward citation searches were conducted on 11th August 2018, using Scopus, Web of Science, and Google Scholar.

The following grey literature sources were searched: grey literature databases (OpenGrey, and ProQuest database for dissertations and theses), Google and Google Scholar, conferences proceedings, and consultation with experts (see Supplementary file 2 for further details).

**Screening and selection of studies**

Literature search results for all databases were exported to Covidence [43], duplicates were removed, and studies were screened and selected. Two researchers independently screened all titles and abstracts for relevance, and disagreements were resolved by discussion. Articles that met the inclusion criteria, or where there was any uncertainty, were obtained in complete form. Full text reports were then independently examined against the inclusion criteria by one researcher, who examined them all, and two postgraduate researchers from the University of Bath, who each examined 50%. Any remaining disagreements were resolved by discussion between two researchers.

**Data extraction**

Data extraction was conducted by one researcher using a data extraction form, with 20% verified by another researcher (see Supplementary file 3 for the data extraction form). No discrepancies were found. Details from all data extraction forms were subsequently entered into an Excel spreadsheet, in preparation for analysis. Raw data were not analysed for this systematic review. However, where there was the potential to attain data in a more relevant format, authors of studies were contacted.

**Quality assessment of included studies**
The AXIS tool [44] was chosen to assess both risk of bias and quality, for the purpose of information and synthesis, and not to exclude studies from this systematic review. The AXIS tool comprises 20 items, most of which were relevant for the descriptive cross-sectional studies likely to comprise the majority of studies in this systematic review. Different study designs have the potential for different biases, and the three main potential biases in cross-sectional and descriptive studies pertain to the proper selection of the sample (selection bias), the soundness of outcome measurement (measurement bias), and the selective reporting of findings (reporting bias) [45-48]. The AXIS tool comprises subscales for separately measuring risk of bias, quality of reporting, and quality of study design. The risk of bias items allow for the measurement of selection bias, measurement bias, and reporting bias.

Each included study, for which there was a full report of the study that was written in English, was independently appraised for quality by two researchers. Only full reports were appraised, since they contained enough information to adequately assess the risk of bias and the quality of reporting. Disagreements were resolved through discussion between two researchers.

**Narrative synthesis**

Findings were synthesised in a narrative synthesis around the study objectives. The narrative synthesis was undertaken based upon the guidelines of Popay et al. [49]. Due to heterogeneity in the services evaluated and the research methodologies employed, meta-analysis was not considered appropriate. However, where relevant, weighted averages were calculated across studies to account for the potential impact of varying sample sizes.

**RESULTS**

**Study selection**

A total of thirty-two studies were identified for inclusion in this review. Figure 1 shows a flow diagram of the study selection process.
Study characteristics

All of the included studies are summarised in Table 1. Of the thirty-two included studies, seventeen studies contained data that examined a MISGP (53%) and fifteen studies contained data that examined a PMHS (47%). Seventeen were published studies in peer-reviewed journals (53%), and fifteen were conference abstracts (47%).

Of the thirty-two studies, eighteen were evaluating services in the UK (56%), six were evaluating services in North America (19%), five were evaluating services in other countries within Europe (16%), and three were evaluating services in other areas of the world (9%).

Four study designs have been used to examine the effectiveness of PMHS and MISGP: cross-sectional surveys of service users (twenty-seven studies; 84%), retrospective review of enquiries (seven studies; 22%), retrospective reviews of answers using expert panels (four studies; 13%), and cross-sectional surveys of service providers (one study; 3%). Six studies had more than one design (19%).

Quality assessment and risk of bias within studies

Sixteen studies met our criteria for quality and risk of bias assessment (i.e., a full report, written in English). Fleiss Kappa was conducted, showing that there was substantial agreement between raters [50], $K = .63$ (95% CI, .53 to .73), $p = .000$.

The mean percentage for overall quality for the sixteen assessed studies was 51% (range = 25%-95%). For the Risk of Bias subscale, the mean percentage for risk of bias across the studies was 63% (range =17%-100%). For the Quality of Reporting subscale, the mean percentage across the studies was 59% (range = 14%-100%). For the Quality of Study Design subscale, the mean percentage across the studies was 55% (range = 29%-100%) (See Supplementary file 4 for the overall scores and percentages of quality and risk of bias for all sixteen studies).

Effectiveness of PMHS and MISGP

Service users’ perceptions of using a PMHS or MISGP
Twenty-two studies examined services users' perceptions of using PMHS and MISGP, using self-report survey methods. Twelve studies examined a MISGP and ten examined a PMHS. Nineteen outcomes were reported, and are presented in Table 2. More outcomes were reported for PMHS than for MISGP (fourteen and eleven, respectively). Most outcomes were reported by a high percentage of enquirers (typically, 90% and above).

Two studies reported negative feedback from survey respondents [51, 52]. Bramley and Hollamby [51] surveyed 97 patients who used one of several PMHS in London between 2011 and 2013. Negative feedback reported by service users were: being provided with insufficient information; feeling that they did not gain anything from calling the helpline, since they were referred to their GP; being told to contact another person, which prolonged the process; and being advised with unclear language. However, the authors did not report actual percentages of participants who were affected by each of these issues.

Out of 67 service users surveyed by Bramley et al. [52], 15% (n = 10) disclosed issues with the PMHS they used. Three patients reported that the helpline advisor could not answer their question, three patients were referred to somebody who could not help them, two patients said that they were not counselled on potential side effects, one patient felt confused by the advice, and one patient reported being given irrelevant advice.

**Impact of using a PMHS or MISGP for service users**

**Service users’ perceptions of the impact of using a PMHS or MISGP**

Twenty-one studies examined service users’ perceptions of the positive impact of using a PMHS or MISGP, using self-report survey methods. Eleven studies examined a MISGP and ten examined a PMHS. Sixteen outcomes were reported, and the findings are presented in Table 3. More outcomes were reported for PMHS than for MISGP (sixteen and eight, respectively).
Four studies reported whether there were negative outcomes for the patient/enquirer’s health, wellbeing or symptoms that could be directly attributed to using the MI service. For PMHS, one study found that there were no reported negative effects [53], and another study found that, out of 58 respondents, 6% reported some negative impact on social wellbeing and physical wellbeing, and 4% reported some negative impact on emotional wellbeing [54]. Additionally, a quarter of their sample felt more anxious after using a PMHS (exact percentage not reported) [54].

For MISGP, one study found that, out of 920 respondents, 1% reported poorer health [55], and another study found that, out of 123 respondents, 5% reported that their condition was worse [56].

**Use of expert panels to examine the impact of PMHS and MISGP**

Two studies included a design whereby an expert panel reviewed enquiries and answers provided by a PMHS [52, 57]. In one of the studies, the expert panel comprised three independent experts in medicine, pharmacology and patient safety methodology [57], and in the other study the expert panel comprised twelve MI pharmacists [52]. For the two studies, the panels agreed that there was a potential positive impact on patient care or outcome in 74% and 89% of cases (n = 46/62 and n = 16/18, respectively), and that there was a potential positive impact on medication safety in 71% and 78% of cases (n = 44/62 and n = 14/18, respectively).

Two studies included a design whereby an expert panel reviewed enquiries and answers provided by a MISGP [58, 59]. Melnyk et al. [59] used an expert panel (two clinical pharmacists and two physicians experienced in general medicine) to classify the potential impact on patient outcome of responses to sixty-eight enquiries to a MISGP in Canada. None of the responses were considered to result in a negative outcome. There were 25 potential positive patient outcomes (37%). Of the queries that potentially resulted in a positive patient outcome, medication administration may have been optimised in 44% of cases, there may have been a reduction/elimination of symptoms in 44% of cases, and there may have been a prevention of disease/symptoms in 12% of cases.
Rhodes et al. [58] used an expert panel (membership not reported) to evaluate the perceived impact of 200 enquiries to a MISGP in France. They found that 81% of responses to enquiries were evaluated as potentially having a significant, very significant, or vital impact (n = 162/200). The remaining 19% were evaluated as having no significant impact (n = 38/200).

**Preventing harm from medicines**

One study examined the potential for harm pertaining to the enquiries received by a PMHS [60]. This was achieved by coding 500 calls as to whether or not they pertained to harm (harm was defined as temporary or permanent impairment of the physical, emotional or psychological function or structure of the body and/or pain resulting therefrom, requiring intervention). Findings identified that 48% of enquiries were judged to have the potential for harm from the medicine/s in question. Of these, 17% were then categorised as Harm Index Category F (requiring intervention and referral), 19.9% were categorised as Harm Index Category E (temporary harm not requiring follow-up), and 78.4% were categorised as Harm Index Categories B-D (an error occurred, but did not cause harm). This suggests that PMHS have the potential to prevent medicines-related harm to patients. However, a limitation of this study is that only one researcher (expertise not reported) coded the enquiries.

**Correcting medicines-related errors**

Six studies reported data from retrospective reviews of enquiries to PMHS, to establish the percentage that were regarding medication errors [57, 60-64]. Combined, the studies found that between 8% and 39% of calls to PMHS concerned errors (mean = 26%; weighted mean = 28%). This suggests that correcting errors is an important function of PMHS. However, it is unknown whether different definitions of an error were used across the studies, which may have influenced the results. Additionally, one study reported that only one researcher coded enquiries [60], and the remaining five studies did not report the number of coders used.

**Reducing the burden upon other healthcare services**
Six studies reported the percentages of service users who would use alternative healthcare professionals/services had the MI service not been available; two examining PMHS [53, 64] and four examining MISGP [56, 65-67]. The findings are presented in Table 4. Additionally, out of 920 respondents Maywald et al. found that 18% of callers to a MISGP in Germany believed that the advice they received prevented a visit to their physician [55].

**Economic impact**

Two studies explored the economic impact of MISGP. Both studies were available as conference abstracts only, therefore their descriptions were limited.

Alomi et al. (2015) sought to establish the cost-efficiency of a national MISGP in Saudi Arabia, by analysing all calls in 2014 and predicting the cost for each had the service not been available [68]. They estimated that the cost avoidance of answering public enquiries for one year was $80,806. However, they did not provide details as to how this was assessed.

Rhodes et al. (2017) conducted an analysis of 200 calls received in 2016 to a national MISGP in France. Using an expert panel, they concluded that 25% of calls to the service had an economic impact, although they do not report what impact, nor the monetary value of the impact.

**Service providers’ opinions as to the effectiveness of their service**

Williams et al. (2018) surveyed pharmacy professionals (MI Pharmacists and Chief Pharmacists) in 2017 for their perceptions regarding the major benefits of their helpline service. The top ten perceived benefits were: avoiding harm to patients (88%; n = 137/156), improving patient medication adherence (85%; n = 133/156), providing assurance to patients that they can access professional help from home (83%; n = 129/156), improving the patient experience (80%; n = 125/156), supporting patient discharge (76%; n = 119/156), optimising medicines (75%; n = 117/156), identifying errors (75%; n = 117/156), reducing medicines-related readmissions (65%; n = 101/156), learning from adverse patient experiences (55%; n = 86/156), and reducing visits to other
healthcare services (51%; n = 80/156). However, a limitation of this study as a measure of
effectiveness is that it relied upon the perceptions of service providers rather than a direct measure.
Results also may be biased if participants were apprehensive about reporting any negative or poor
aspects of their service.

DISCUSSION

This systematic review examined the available evidence regarding the effectiveness of
medicines information services for patients and the general public. The evidence suggests that both
PMHS and MISGP may help to increase service users’ knowledge, understanding and use of their
medicines, and that advice is typically reported as being followed. Both PMHS and MISGP are
typically perceived as positive by service users (e.g., satisfaction ratings are typically very high), and
service users may report several positive outcomes attributed to using PMHS such as problems being
resolved or avoided, and experiencing improvements to their health.

Studies also suggest that both PMHS and MISGP may have an impact upon other healthcare
services, such as reducing the burden upon primary care (i.e., if the helpline did not exist,
respondents report that they would likely contact their GP instead; weighted mean for PMHS = 41%;
weighted mean for MISGP = 38%). This is topical, given that the average waiting time from booking a
standard appointment to seeing a GP in England in 2016 and 2017 was estimated to be
approximately two weeks [69]. This suggests that, by increasing patients’ and carers’ awareness of
MI services that are available to them, patients can receive support much sooner than if they book
an appointment to see their GP, and GP time will be less taken up with answering MI queries that
may be more appropriately dealt with via MI pharmacists.

Although a larger number of studies have been conducted to examine a MISGP compared
with a PMHS, more outcomes have been reported for PMHS than for MISGP. Of those outcomes
reported for both service types, some outcomes are superior for PMHS whereas other outcomes are
superior for MISGP. However, it is not legitimate to draw comparisons between the effectiveness of the two service types based upon the available evidence in this review, since no evidence was found that compared the two service types within the same study. Additionally, a comparison between the two service types may be inappropriate, since their functions are not exactly the same. A recent study by Badiani et al. [62] found that, out of 200 enquiries to their PMHS, 75% required access to hospital-based resources (e.g., patients’ electronic medical records, and contacting a healthcare professional involved in the patient’s care). Badiani et al. conclude that their findings support the value of hospitals providing a PMHS for their own patients, rather than having a smaller number of centralised MI services for all individuals within a region. It may be that MISGP are suitable for more general enquiries that do not require access to a patients’ record (e.g., enquiries pertaining to over-the-counter medicines), whereas PMHS may be more suitable for more complex enquiries pertaining to medicines specifically prescribed from the hospital where the enquirer recently received care. Future research could aim to establish this by examining the types of enquiries made to the two different services. Due to their different functions, it may be that providing patients and the general public with both PMHS and MISGP, whether separately or combined, is useful for supporting them regarding all types of medicines-related queries.

A potential strength of the available evidence is that several different study designs have been used to examine the effectiveness of MI services, including retrospective reviews of enquiries, use of expert panels, and cross-sectional surveys with service users and service providers. However, the use of a variety of study designs can only be considered a strength if the studies themselves are methodologically robust and of a high quality. We found that the overall quality of the evidence was moderate (on average, 51%), and there was a high risk of bias in study articles (on average, 63%). Most of the included studies were service evaluations whereby study authors had evaluated their own service. Additionally, evidence was primarily based upon self-report methods, and such findings may be subject to bias since service users’ perceptions of impact may not be the same as actual
impact. A small number of studies have also been conducted using expert panels, and these also report PMHS and MISGP to have a positive impact on patient outcomes. However, expert panels require expertise in judging both the nature of the enquiry and the appropriateness of the response in the context in which it is made, and such details were not always explicitly reported in the included studies. This review highlights the need for more high-quality research to adequately evaluate the impact of these services.

**Recommendations**

**Practice**

The evidence from this review shows that PMHS and MISGP may have a number of benefits for service users and healthcare organisations. Healthcare organisations that currently do not provide an MI service to patients and/or the public should consider whether the evidence is sufficient to merit developing their own.

We encourage MI service providers to evaluate the types of enquiries they receive by using standardised categories and coding instructions/training (e.g., those that were developed by the UK Medicines Information network; UKMi). This will enable the types of enquiries to be more appropriately compared across sites and regions within a country, and across countries. Relatedly, the wide variety in error rates found across studies in this review (i.e., 8% – 39%) may reflect the use of different definitions as to what constitutes a medicines-related error, since the definition of an error has been found to have an effect upon rates [70, 71]. We therefore also recommend that sites use a standardised definition of ‘medicines-related error’, including a standardised categorisation/coding scheme for collecting and analysing enquiry data.

**Future research**
Further research is needed to examine the effectiveness of both PMHS and MISGP (both in the UK and internationally), and we encourage researchers to use the findings from this review to design and conduct high-quality studies that fill gaps in the evidence-base for both types of service.

In the UK, the UKMi provide an example survey to collect feedback regarding service users’ experiences of using PMHS [25]. This tool was used in several of the studies included in this review. However, the psychometric properties of the tool have not been evaluated, and its reliance upon checkboxes may produce misleading results. It would therefore be beneficial for a psychometrically robust survey tool to be developed in order to more adequately examine service users’ perspectives regarding the effectiveness of PMHS and MISGP.

The evidence in this review is compiled predominantly from studies conducted by sites that have examined their own service, which may not be generalisable and are at a high risk of bias. For both types of services, independently-conducted, larger, and higher-quality multi-centre studies are needed to examine their effectiveness. Relatedly, the average response rate for cross-sectional surveys completed by service users in this review was 55%, and reported response rates were often calculated based upon the number of responses received out of the total number of callers who were asked and who agreed to participate. Therefore, it is questionable as to whether the positive findings regarding the effectiveness of PMHS and MISGP are generalisable if, for example, those who had a negative experience chose not to respond, or were not asked to participate in the first place.

Future research could seek to improve the generalisability of survey studies by inviting all callers during the recruitment phase of the study. Examples of ways to improve response rates include offering an incentive, providing respondents with different modes of completing the survey (i.e., postal and online), and by resending the survey to non-responders [72].

Only six of the thirty-two studies that examined the effectiveness of PMHS and MISGP provided data regarding perceived negative opinions/outcomes of the service. One study found that 15% of service users felt more anxious after using a PMHS, although the study authors did not
explore reasons for these findings [54]. Therefore, further research could seek to examine both positive and negative aspects of service users’ experiences. For example, qualitative interviews with service users could be beneficial for exploring in greater depth the experiences of patients and the general public regarding their use of a PMHS or a MISGP. This could help to understand why some callers report feeling more anxious after using a PMHS, and potentially detect other adverse effects that may not be captured in surveys. Qualitative methods would also be useful for establishing what patients and the general public want from an MI service, and whether there are specific ways that PMHS and MISGP could be improved to better suit their needs.

Future research could also examine whether PMHS and MISGP have the potential to reduce hospital readmission rates, and the extent that the reduced burden upon other healthcare services (e.g., emergency departments, primary care services) translates into cost savings. Two studies sought to examine the cost efficiency of MISGP. However, the available evidence was limited, since the studies were conference abstracts. Such findings could help support sustainable funding models, thus improving the adoption and maintenance of MI services for patients and the general public [73].

Strengths and limitations

This is the first systematic review that has examined the effectiveness of MI services for patients and the general public. We have identified, synthesised, and appraised a large body of evidence regarding MI services for both patients and the general public from countries worldwide. This has resulted in our development of recommendations to improve current practice in the operation of MI services, and for areas for future research.

One limitation of this systematic review is that the tool selected to assess the quality and risk of bias of studies was new, and consequently, its psychometric properties had not been evaluated [44]. This may have affected the inter-rater agreement that was conducted for this review. However, we found that our inter-rater agreement was satisfactory [74]. Additionally, the
issue of lack of psychometric evaluation was common to all of the tools we considered for use in this study to assess quality and risk of bias. Systematic reviews of tools for assessing quality and risk of bias have concluded that there is no single obvious candidate tool for assessing the risk of bias or quality in cross-sectional studies [75-77].

Relatedly, only sixteen of the thirty-two studies in this review met our eligibility criteria for the assessment of quality and risk of bias, since most studies were from conference abstracts. Of the sixteen studies, on average, their quality was found to be moderate (51%; range = 25%-95%) and their risk of bias was found to be high (63%; range =17%-100%). Therefore, the findings may be limited due to the lack of high-quality studies currently available.

Another limitation of this review is that we only included articles written in non-English languages where the abstract was reported in the English language, if the abstract alone provided information to support our research objectives. Therefore, it may be that some relevant articles were excluded from this review. However, the maximum number of articles that this could have applied to was six (out of 8676). Additionally, the search for studies for this review was conducted in August 2018. It is possible that other studies may have subsequently been published which could affect the overall findings.

Finally, this systematic review combined the results for MISGP across countries (e.g., USA, Canada, Germany, France, Netherlands, Israel, Saudi Arabia). It is possible that differences may exist regarding the provision of MISGP by each of these countries, which may have affected the pooled findings in our review. However, the aim of our review was to provide an overview of the effectiveness of MISGP as a starting point for future research to build upon.

Conclusions

This systematic review provides evidence to suggest that PMHS and MISGP may be a beneficial source of support for recently discharged hospital patients and the general public,
respectively. Overall, the quality of studies was found to be moderate, and there was a high risk of bias in the included studies. Most studies were service evaluations conducted by the providers of their own service. Therefore, more high-quality research is needed to build the evidence-base regarding the effectiveness of both types of services, ideally by researchers who are independent of the services being studied. This will enable healthcare commissioners and providers to be better informed to make decisions regarding robust MI service design and delivery.

LIST OF ABBREVIATIONS

NHS = National Health Service; PMHS = patient medicines helpline service; MISGP = medicines information service for the general public; UK = United Kingdom; MI = medicines information; UKMI = United Kingdom Medicines Information Network.

DECLARATIONS

Ethics approval and consent to participate
Not applicable, since the research used secondary data sources collected from published and unpublished studies.

Consent for publication
Not applicable.

Availability of data and material
Not applicable, since no primary data were collected or used for this research.

Competing interests
The authors declare that they have no competing interests.

Funding
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Endnotes

1. The National Health Service (NHS) in England is organised into NHS Trusts, which are organisations that provide goods and services for the purposes of health care (e.g., hospital and community services), and each Trust primarily serves a geographical area within England.

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51. Bramley D, Hollamby M. How can we improve and learn from previous patient helpline enquiries and their feedback? Poster session presented at: 41st UKMi Practice Development Seminar; 2015 Sep 11; East Midlands, UK.

53. McCartan C. *Implementation and evaluation of a pilot medicines helpline for patients discharged from the Belfast Health and Social Care Trust.* Poster session presented at: 42nd UKMi Practice Development Seminar; 2016 Sep 27; Birmingham, UK.


63. Law S. *Development and analysis of the patient medicines helpline.* Poster session presented at: 41st UKMi Practice Development Seminar; 2015 Sep 11; East Midlands, UK.

64. Jones M, Pettitt P. *The use of outcome data monitoring in the quality assurance of MI services.* Poster session presented at: 40th UKMi Practice Development Seminar; 2014 Sep 12; Birmingham, UK.


79. Barker L, Badiani A. What do patients think of the UHS medicines helpline? Poster session presented at: 42nd UKMi Practice Development Seminar; 2016 Sep 27; Birmingham, UK.


Additional files

File name: Supplementary file 1.

File format: .pdf

Title of data: Search strategy for EMBASE
Description of data: Search strategy for EMBASE

File name: Supplementary file 2.
File format: .pdf
Title of data: Grey literature search strategy
Description of data: Grey literature search strategy

File name: Supplementary file 3.
File format: .pdf
Title of data: Data extraction form
Description of data: Data extraction form

File name: Supplementary file 4.
File format: .pdf
Title of data: Quality assessment and risk of bias
Description of data: Quality assessment and risk of bias table
Table 1. Studies meeting the eligibility criteria for the systematic review examining medicines information services for patients and the public.

<table>
<thead>
<tr>
<th>First author, Year</th>
<th>Publication status</th>
<th>Study design/s</th>
<th>Service type</th>
<th>Country</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alomi, 2015 [68]</td>
<td>CA</td>
<td>RRE</td>
<td>MISGP</td>
<td>Saudi Arabia</td>
<td>NR</td>
</tr>
<tr>
<td>Ansani, 2006 [78]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>USA</td>
<td>6 respondents</td>
</tr>
<tr>
<td>Badiani, 2017 [62]</td>
<td>PS-PR</td>
<td>RRE; SSU</td>
<td>PMHS</td>
<td>England</td>
<td>637 enquiries; 100 respondents</td>
</tr>
<tr>
<td>Barker, 2016 [79]</td>
<td>CA</td>
<td>SSU</td>
<td>PMHS</td>
<td>England</td>
<td>9 respondents</td>
</tr>
<tr>
<td>Blom, 1991 [65]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>Netherlands</td>
<td>200 respondents</td>
</tr>
<tr>
<td>Bramley, 2012 [80]</td>
<td>CA</td>
<td>SSU</td>
<td>PMHS</td>
<td>England</td>
<td>73 respondents</td>
</tr>
<tr>
<td>Bramley, 2014 [61]</td>
<td>PS-PR</td>
<td>RRE</td>
<td>PMHS</td>
<td>England</td>
<td>312 enquiries</td>
</tr>
<tr>
<td>Bramley, 2014 [81]</td>
<td>CA</td>
<td>SSU</td>
<td>PMHS</td>
<td>England</td>
<td>17 respondents</td>
</tr>
<tr>
<td>Bramley, 2015 [51]</td>
<td>CA</td>
<td>SSU</td>
<td>PMHS</td>
<td>England</td>
<td>97 respondents</td>
</tr>
<tr>
<td>Conner, 1980 [82]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>USA</td>
<td>73 respondents</td>
</tr>
<tr>
<td>Conner, 1982 [83]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>USA</td>
<td>793 respondents</td>
</tr>
<tr>
<td>Cuthbert, 2013 [57]</td>
<td>CA</td>
<td>RRE; RRA-EP; SSU</td>
<td>PMHS</td>
<td>Scotland</td>
<td>18 enquiries; 17 respondents</td>
</tr>
<tr>
<td>Goltz, 2009 [84]</td>
<td>CA</td>
<td>SSU</td>
<td>MISGP</td>
<td>Germany</td>
<td>151 respondents</td>
</tr>
<tr>
<td>Goltz, 2011 [85]</td>
<td>CA</td>
<td>SSU</td>
<td>MISGP</td>
<td>Germany</td>
<td>496 respondents</td>
</tr>
<tr>
<td>Heaton, 2018 [86]</td>
<td>CA</td>
<td>SSU</td>
<td>PMHS</td>
<td>England</td>
<td>20 respondents</td>
</tr>
<tr>
<td>Jones, 2014 [64]</td>
<td>CA</td>
<td>RRE; SSU</td>
<td>PMHS</td>
<td>England</td>
<td>234 enquiries; 68 respondents</td>
</tr>
<tr>
<td>Law, 2015 [63]</td>
<td>CA</td>
<td>RRE</td>
<td>PMHS</td>
<td>England</td>
<td>109 enquiries</td>
</tr>
<tr>
<td>Markovits, 2011 [87]</td>
<td>CA</td>
<td>SSU</td>
<td>MISGP</td>
<td>Israel</td>
<td>30 respondents</td>
</tr>
<tr>
<td>Marvin, 2011 [60]</td>
<td>PS-PR</td>
<td>RRE</td>
<td>PMHS</td>
<td>England</td>
<td>500 enquiries</td>
</tr>
<tr>
<td>Maywald, 2004 [55]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>Germany</td>
<td>920 respondents</td>
</tr>
<tr>
<td>McCartan, 2016 [53]</td>
<td>CA</td>
<td>SSU</td>
<td>PMHS</td>
<td>Northern Ireland</td>
<td>14 respondents</td>
</tr>
<tr>
<td>Melnyk, 2000 [88]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>Canada</td>
<td>99 respondents</td>
</tr>
</tbody>
</table>
Running Head: Effectiveness of medicines information services

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Publication Status</th>
<th>Study Design</th>
<th>Country</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melnyk, 2000 [59]</td>
<td>PS-PR</td>
<td>RRA-EP; SSU</td>
<td>MISGP</td>
<td>Canada</td>
<td>68 enquiries; 64 respondents</td>
</tr>
<tr>
<td>Muhammad, 1998 [66]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>England</td>
<td>57 respondents</td>
</tr>
<tr>
<td>Olofinjana, 2009 [56]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>UK</td>
<td>123 respondents</td>
</tr>
<tr>
<td>Raccah, 2011 [89]</td>
<td>CA</td>
<td>SSU</td>
<td>MISGP</td>
<td>England</td>
<td>268 respondents</td>
</tr>
<tr>
<td>Rhodes, 2017 [58]</td>
<td>CA</td>
<td>RRA-EP; SSU</td>
<td>MISGP</td>
<td>France</td>
<td>200 enquiries; 149 responders</td>
</tr>
<tr>
<td>Rutter, 2012 [90]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>UK</td>
<td>77 respondents</td>
</tr>
<tr>
<td>Smith, 1985 [67]</td>
<td>PS-PR</td>
<td>SSU</td>
<td>MISGP</td>
<td>USA</td>
<td>154 respondents</td>
</tr>
<tr>
<td>Williams, 2018 [23]</td>
<td>PS-PR</td>
<td>SSP</td>
<td>PMHS</td>
<td>England</td>
<td>156 respondents</td>
</tr>
</tbody>
</table>

*Note. General abbreviations: PMHS = patient medicines helpline service; MISGP = medicines information service for the general public; NR = not reported. 'Publication status' abbreviations: PS-PR = published study in a peer reviewed journal; CA = conference abstract. 'Study design' abbreviations: RRE = retrospective review of enquiries; RRA-EP = retrospective review of answers by expert panel; SSU = cross-sectional survey of service users; SSP = cross-sectional survey of service providers. All studies evaluated services that were accessed via telephone, except the service evaluated by Ansani et al., which was accessed online.*
Table 2. Services users’ perceptions of using medicines information services for patients and the general public

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patient medicines helpline services</th>
<th>Medicines information services for the public</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. studies examining outcome</td>
<td>Range of % (mean; WM)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range of N (total N)</td>
</tr>
<tr>
<td>Felt understood</td>
<td>4 [52, 62, 79, 80]</td>
<td>99% - 100% (100%)</td>
</tr>
<tr>
<td>Would use service again</td>
<td>5 [52, 62, 79, 81, 86]</td>
<td>94% - 100% (98%; 99%)</td>
</tr>
<tr>
<td>Able to understand information/advice</td>
<td>2 [52, 80]</td>
<td>97% - 100% (99%; 98%)</td>
</tr>
<tr>
<td>Felt confident in answer provided</td>
<td>3 [53, 62, 79]</td>
<td>98% - 100% (99%; 98%)</td>
</tr>
<tr>
<td>Experience of hospital was improved</td>
<td>1 [64]</td>
<td>98%</td>
</tr>
<tr>
<td>Service was helpful a</td>
<td>6 [53, 54, 62, 64, 79, 80]</td>
<td>88% - 100% (97%; 96%)</td>
</tr>
<tr>
<td>Enough information was provided</td>
<td>2 [52, 62]</td>
<td>93% - 98% (96%; 96%)</td>
</tr>
<tr>
<td>Information was timely</td>
<td>3 [80, 81, 86]</td>
<td>76% - 100% (91%; 94%)</td>
</tr>
<tr>
<td>Satisfied with the service b</td>
<td>2 [54, 57]</td>
<td>92% - 100% (96%; 94%)</td>
</tr>
<tr>
<td>No improvements to service needed</td>
<td>2 [57, 80]</td>
<td>88% - 94% (91%; 89%)</td>
</tr>
<tr>
<td>Service was useful c</td>
<td>1 [52]</td>
<td>88%</td>
</tr>
</tbody>
</table>

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### Effectiveness of medicines information services

<table>
<thead>
<tr>
<th>Access to service was easy</th>
<th>5 [52-54, 62, 79]</th>
<th>61% - 100% (88%; 85%)</th>
<th>9 - 100 (235)</th>
<th>0</th>
<th>N/A</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Service was excellent</td>
<td>3 [52, 62, 79]</td>
<td>61% - 80% (73% 73%)</td>
<td>9 - 100 (176)</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Given additional information</td>
<td>2 [57, 80]</td>
<td>14% - 47% (31%; 20%)</td>
<td>17 - 73 (90)</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Information provided was relevant</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
<td>1 [58]</td>
<td>100%</td>
<td>149</td>
</tr>
<tr>
<td>Would recommend service</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
<td>2 [78, 90]</td>
<td>83%-100% (92%; 99%)</td>
<td>6 - 77 (83)</td>
</tr>
<tr>
<td>The advisors were competent</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
<td>1 [55]</td>
<td>69%</td>
<td>920</td>
</tr>
<tr>
<td>The service was thorough</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
<td>1 [55]</td>
<td>52%</td>
<td>920</td>
</tr>
<tr>
<td>Useful to be able to obtain second opinion</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
<td>1 [55]</td>
<td>40%</td>
<td>920</td>
</tr>
</tbody>
</table>

**Note.** Abbreviations: WM = weighted mean (weighted by sample size); N/A = no relevant data were found for these categories. Nineteen studies examined self-reported outcomes for enquirers of medicines information services. Therefore, some studies reported more than one type of outcome. Outcomes are listed according to the weighted mean percentage for studies that examined PMHS, from largest to smallest.

a Due to different answer options being used across studies, for some studies 'helpful' and 'very helpful' were added together to produce the percentage of service users that found the service to be helpful.

b Due to different answer options being used across studies, for some studies 'satisfied' and 'very satisfied' were added together to produce the percentage of service users that were satisfied with the service.

c Due to different answer options being used across studies, for some studies 'useful' and 'very useful' were added together to produce the percentage of service users that found the service to be useful.
Table 3. Services users' perceptions of the impact of using medicines information services for patients and the general public

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patient medicines helpline services</th>
<th>Medicines information services for the public</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. studies examining outcome</td>
<td>Range of % (mean; WM)</td>
</tr>
<tr>
<td>Recommendations were followed</td>
<td>5 [52, 54, 57, 64, 80]</td>
<td>88% - 100% (93%; 94%)</td>
</tr>
<tr>
<td>Benefit experienced (unspecified)</td>
<td>1 [52]</td>
<td>86%</td>
</tr>
<tr>
<td>An issue/problem was resolved</td>
<td>5 [53, 62, 64, 79, 86]</td>
<td>33% - 100% (65%; 66%)</td>
</tr>
<tr>
<td>Feeling reassured or less anxious after using the service</td>
<td>9 [52-54, 57, 62, 64, 79-81]</td>
<td>38% - 100% (67%; 65%)</td>
</tr>
<tr>
<td>Feeling more confident taking medicines after using the service</td>
<td>1 [81]</td>
<td>65%</td>
</tr>
<tr>
<td>Increased knowledge/understanding of medicines</td>
<td>5 [52, 57, 64, 80, 81] *</td>
<td>31% - 82% (63%; 55%)</td>
</tr>
<tr>
<td>Belief that harm was avoided</td>
<td>2 [57, 80]</td>
<td>43% - 59% (51%; 46%)</td>
</tr>
<tr>
<td>Information provided was used to make a decision about medicines</td>
<td>1 [52]</td>
<td>43%</td>
</tr>
<tr>
<td>Patient able to start taking their medicines after using the service</td>
<td>1 [53]</td>
<td>43%</td>
</tr>
<tr>
<td>A problem was avoided</td>
<td>3 [53, 54, 62]</td>
<td>21% - 67% (38%; 40%)</td>
</tr>
<tr>
<td>Improvement in health, wellbeing, or symptoms after using the service</td>
<td>6 [52-54, 57, 64, 80]</td>
<td>7% - 83% (34%; 34%)</td>
</tr>
</tbody>
</table>
Treatment was changed as a result of using the service | 5 [52, 53, 57, 64, 80] | 13% - 53% (29%; 27%) | 14 - 73 (231) | 2 [56, 89] | 41% - 47% (44%; 43%) | 123 - 268 (391)
---|---|---|---|---|---|---
Patient changed or improved the way they take their medicines | 3 [53, 64, 81] | 6% - 76% (34%; 27%) | 14 - 68 (99) | 0 | N/A | N/A
Patient more likely to take their medicines regularly | 2 [64, 81] | 6% - 53% (30%; 15%) | 17 - 68 (85) | 0 | N/A | N/A
Patient less likely to miss a dose | 2 [80, 81] | 4% - 41% (23%; 13%) | 17 - 54 (71) | 0 | N/A | N/A
Patient able to obtain a supply of their medicines after using the service | 2 [53, 64] | 10% - 12% (11%; 10%) | 14 - 68 (82) | 0 | N/A | N/A

*Note.* Abbreviations: WM = weighted mean percentage (weighted by sample size); N/A = no relevant data were found for these categories.

Seventeen studies examined self-reported outcomes for enquirers of medicines information services. Therefore, some studies reported more than one type of outcome. Outcomes are listed according to the weighted mean percentage for studies that examined PMHS, from largest to smallest.

*Jones et al., provided additional detail about the type of knowledge that was increased [80]. Thirty-one percent reported an increased understanding of interactions, 18% reported an increased understanding of side effects and safety, 15% reported an increased understanding of how to take their medicines, and 9% reported an increased understanding of supplies, changes to their medicines, and indications.*
### Table 4. Services users' suggested sources of support from healthcare professionals/service had their medicines information service not been available.

<table>
<thead>
<tr>
<th>Healthcare service/professional contacted if MI service was not available</th>
<th>Patient medicines helpline services</th>
<th></th>
<th></th>
<th>Medicines information services for the public</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. studies examining outcome</td>
<td>Range of % (mean; WM)</td>
<td>Range of N (total N)</td>
<td>No. studies examining outcome</td>
<td>Range of % (mean; WM)</td>
</tr>
<tr>
<td><strong>GP</strong></td>
<td>2 [53, 64]</td>
<td>36% - 65% (51%; 41%)</td>
<td>14 - 68 (82)</td>
<td>4 [56, 65-67]</td>
<td>15% - 58% (40%; 38%)</td>
</tr>
<tr>
<td><strong>Hospital where they received care</strong></td>
<td>2 [53, 64]</td>
<td>29% - 31% (30%; 29%)</td>
<td>14 - 68 (82)</td>
<td>1 [66]</td>
<td>6%</td>
</tr>
<tr>
<td><strong>Pharmacist</strong></td>
<td>2 [53, 64]</td>
<td>7% - 40% (24%; 13%)</td>
<td>14 - 68 (82)</td>
<td>4 [56, 65-67]</td>
<td>10% - 62% (31%; 34%)</td>
</tr>
<tr>
<td><strong>Other healthcare professional / service</strong></td>
<td>1 [64] $^{a}$</td>
<td>10%</td>
<td>68</td>
<td>2 [56, 67]</td>
<td>8% - 11% (10%; 9%)</td>
</tr>
<tr>
<td><strong>Would go without help</strong></td>
<td>2 [53, 64]</td>
<td>3% - 14% (9%; 5%)</td>
<td>14 - 68 (82)</td>
<td>3 [65-67]</td>
<td>12% - 23% (16%; 17%)</td>
</tr>
<tr>
<td><strong>Nurse</strong></td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
<td>2 [66, 67]</td>
<td>2% - 10% (6%; 8%)</td>
</tr>
</tbody>
</table>

*Note. Abbreviations: WM = weighted mean percentage (weighted by sample size); N/A = no relevant data were found for these categories. Seventeen studies examined self-reported outcomes for enquirers of medicines information services. Therefore, some studies reported more than one type of outcome. Outcomes are listed according to the weighted mean percentage for studies that examined PMHS, from largest to smallest. $^{a}$ The 'other healthcare professional / service' reported in this study was NHS 111, a national medical helpline in England.*