Written information about individual medicines for consumers (Review)

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[Intervention Review]

Written information about individual medicines for consumers

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Editorial group: Cochrane Consumers and Communication Group.
Publication status and date: Edited (no change to conclusions), published in Issue 11, 2011.
Review content assessed as up-to-date: 28 March 2007.

Citation: Nicolson DJ, Knapp P, Raynor DK, Spoor P. Written information about individual medicines for consumers. *Cochrane Database of Systematic Reviews* 2009, Issue 2. Art. No.: CD002104. DOI: 10.1002/14651858.CD002104.pub3.

ABSTRACT

Background

Medicines are the most common intervention in most health services. As with all treatments, those taking medicines need sufficient information: to enable them to take and use the medicines effectively, to understand the potential harms and benefits, and to allow them to make an informed decision about taking them. Written medicines information, such as a leaflet or provided via the Internet, is an intervention that may meet these purposes.

Objectives

To assess the effects of providing written information about individual medicines on relevant patient outcomes (knowledge, attitudes, behaviours and health outcomes) in relation to prescribed and over-the-counter medicines.

Search methods

We searched MEDLINE, EMBASE, CINAHL, *The Cochrane Library*, PsycINFO and other databases to March 2007. We handsearched five journals' tables of contents, and the reference lists of included studies, and contacted experts in the field.

Selection criteria

Randomised controlled trials (RCTs) of medicine users, comparing written medicines information with no written medicines information; or trials that compared two or more styles of written medicines information. We only included trials that measured a knowledge, attitudinal or behavioural outcome. There were no language restrictions.

Data collection and analysis

Two review authors independently extracted data relating to the interventions, methods of the trials, and outcome measures; and reconciled differences by discussion. Heterogeneity of interventions and outcomes measured meant that data synthesis was not possible. The results are presented in narrative and tabular format.

Main results

We included 25 RCTs involving 4788 participants. Six of twelve trials showed that written information significantly improved knowledge about a medicine, compared with no written information. The inability to combine results means we cannot conclude whether written information was effective for increasing knowledge. The results for attitudinal and behavioural outcomes were mixed. No studies showed an adverse effect of medicines information.

Authors' conclusions

The combined evidence was not strong enough to say whether written medicines information is effective in changing knowledge, attitudes and behaviours related to medicine taking. There is some evidence that written information can improve knowledge. The trials were generally of poor quality, which reduces confidence in the results. Trials examining the effects of written information need to be better designed and use consistent and validated outcome measures. Trials should evaluate internet-based medicines information. It is imperative that written medicines information be based on best practice for its information design and content, which could improve its effectiveness in helping people to use medicines appropriately.

PLAIN LANGUAGE SUMMARY

Written information about individual medicines for patients

Medicines are the most common intervention in most health services. People taking medicines need good quality information: to enable them to take and use the medicines effectively, to understand the potential harms and benefits, and to allow them to make an informed decision about taking them. Written medicines information is provided in some countries as a leaflet accompanying medicines, and is available via the Internet. Our review examined if written information about individual medicines can improve knowledge or attitudes, or change behaviours relating to taking a medicine.

The findings of this review were inconclusive for a number of reasons. First, because the included trials measured different outcomes in different ways, we were unable to combine their results. Second, these trials presented the written information for patients in different ways, and most did not design the leaflets in a way that made them easy to read. Third, in many cases trials were not clearly reported, so we do not know if they were carried out correctly. Despite these limitations several trials, while using different types of information and different measures, found written information improved knowledge. This is encouraging for people who want to learn about their medicines from leaflets. None of the studies showed that written information was harmful.

Future research needs to use improved methods, and needs to examine the same measures on many occasions. It is important that medicines information be well written and designed to maximise the possibility of improving knowledge. Consumers are increasingly seeking out health information, including information about medicines, on the internet, but we found no trials examining whether internet-based medicines information changed people's knowledge, attitudes, or behaviour.

BACKGROUND

Medicines and medicines information

Medicines are the most common intervention in most health services. As with all treatments, those taking medicines need sufficient information: to enable them to take and use the medicines effectively, to understand the potential harms and benefits, and to allow them to make an informed decision about taking them (Raynor 1998).

Evidence-based policy and practice in providing written medicines information (WMI) for patients is a priority for several important reasons. As a European Commission statement (EC 2003) noted: "People are demanding and using health information on an unprecedented scale…linked to a change from the individual as a passive recipient of healthcare and advice, to that of a more empowered and more proactive consumer of healthcare. The aim should be to provide a realistic and practical framework for the provision of information to patients on medicines."

It is estimated that around half of all patients do not take medicines as prescribed (Haynes 2008), leading to wasted resources and sub-optimal health care. Concern with medicine non-compliance was the main stimulus in the 1970s and 1980s for research into patient information needs, and the development of a range of information materials to meet these needs. The assumption was that simply increasing patients' knowledge of treatment would be an effective means of reducing non-compliance, as evidenced by Ley's review (Ley 1988). More recently, an understanding of the complexity of factors underlying patients' use of medicines has developed. It is now recognised that in many cases non-compliance is intentional rather than the result of ignorance, the inability to recall the information, or a misunderstanding (RPSGB 1997). It also appears that self-regulation of medicine-taking by patients is frequently

not shared with doctors (Lowe 2000). Increasingly, patients are recognised as active managers of their own health care, and need to be able to make reasoned decisions about medicine taking in accordance with wider goals and aspirations (Donovan 1992).

Evidence base and legislation

Along with developments in the understanding of patients' use of medicines, legislation and guidelines linked to WMI have emerged in the developed world since the 1990s (Raynor 2003). Different models have been developed, notably in Europe, the US and Australia. European Union (EU) legislation introduced in the 1990s and fully implemented in 1999 requires that a comprehensive medicines information leaflet for patients be supplied inside the pack of every medicine (EC 1992). The leaflets defined by this law are written and supplied by the manufacturer, according to the detail of the legislation, and delivered as a package insert. A key feature of these leaflets is that all information in the Summary of Product Characteristics (intended for health professionals) must be included in the patient leaflet, but in a form comprehensible to the patient. Thus, all warnings, precautions and contra-indications must be included in the leaflet. The result is often a small, thin, folded leaflet, dense with information. More recently, studies have shown that people do not feel that the leaflets meet their needs (Consumers Assoc 2003; Raynor 2004), and most patients do not read the leaflet after the first time of being prescribed a medicine (Raynor 2007a). A subsequent EU Guideline on readability of the leaflets (EC 1998) included recommendations on describing the risk of side effects, and what to do about them, which have since been shown to be ineffective and possibly detrimental (Berry 2002; Berry 2004). Importantly, the Guideline for the first time recommended testing leaflets with patients.

In Australia, law requires that a manufacturer's leaflet is available with all new medicines. A collaborative approach was adopted in the development of the regulations. The leaflets are computer-generated in the pharmacy and can run to five pages (Parker 2001). In the US a voluntary system has prevailed since the 1970s, despite pressure from the Food and Drug Administration (FDA) and consumers (Nightingale 1995). The leaflets are again computer-generated, but are, at one page long, generally briefer than those produced in Australia and Europe. FDA-funded research across eight US states has given the best overview of any of the national initiatives (Svarstad 2003). In 1996 the US legislated a target for the provision of 'useful written information' to 95% of people receiving new prescriptions, by 2006 (Congress 1996; Steering 1996).

The legislated format is not the only form of information about individual medicines available to (and used by) patients (Raynor 1998). Patients may be given additional written information by health professionals, or may access it themselves from other sources including the internet (Dickinson 2003). Our aim was to include research on all such sources of information about individual medicines in the review.

Right to information and concordance

Health policy priorities generally aim to develop higher quality and more responsive services, where patients' wishes and autonomy are respected (NHS 2000). More pragmatically, they also aim to increase efficiency and cost-effectiveness. Providing good quality information about medicines is a prerequisite for informed consent to treatment. It is also seen to underpin genuine choice of treatment for patients and active involvement in managing illness. This characterises the concordant (or partnership) model of medical consultations (RPSGB 1997). Concordance aims to achieve a shared understanding between the patient and prescriber on treatment choices. Patients may be more likely to take medicines when they have been actively involved in treatment decisions. However, there is no evidence that written information alone will increase compliance in long-term therapy (Raynor 1998). Increased knowledge about medicines may support patients' decisions not to take them, as well as to accept them. The goal of concordance is not primarily to increase compliance (though this may be an outcome), but rather to improve the quality of health care by achieving mutual understanding between patients and prescribers, enabling patients to take a more active part in decisions about treatment and illness management when they wish to do so.

A review of existing leaflets revealed many to be medico-centred and biased toward the biomedical model of illness (Dixon-Woods 2001). Coulter 1999 noted that patients expressed a need for information about: what was wrong; the justification and outcomes of tests and treatments; likely illness prognosis; promotion of self care; awareness of services and self-help support; coping strategies; informing others; legitimising help seeking; how to access further information; as well as reassurance. Mental health service users have expressed the need for information in order to understand what medicines they are taking and why, how the medicines act, as well as possible side effects of treatment (Campbell 1998). This review sought to cover all such eligible research that focuses on patient outcomes.

New methods of information delivery

The impact of medicines information produced electronically is starting to be felt. In Australia and the US computer-generated information in the pharmacy is the mainstay and consumers can also now access both official and unofficial information from the internet. In the UK many mandatory leaflets can be viewed online (at www.emc.vhn.net), and new internet-based medicine 'leaflets' called Medicine Guides have been piloted (www.medicines.org.uk). Computer-generated leaflets are promoted as advantageous in terms of being easily updated, individualised and made usable for people with special needs. Any eligible research of electronically generated information about individual medicines was to be included in this review.

Secondary research evidence

This review is based on a larger systematic review of the role, value and effectiveness of WMI for patients which was published as a Health Technology Assessment (HTA) Report (Raynor 2007b). A Cochrane review by Haynes and colleagues (Haynes 2008) on interventions to improve adherence to medication included WMI interventions, but only in a much wider context. The reviews by Buck (Buck 1998) and Koo (Koo 2003) are also relevant to this topic, but neither examines the effectiveness of information provision. Over the last 20 years, a number of non-systematic reviews including policy-related documents (Consumers Assoc 2003; Detmer 2003) have been conducted. Each tends to provide detailed information about specific aspects of providing written information about medicines, including the following:

- Psychological approaches (Ley 1988; Wright 1999), impact on knowledge and compliance (Morris 1979), electronic generation (Kenny 1998), graphical representation (van der Waarde 1993), user testing (Sless 2001), information design (Hartley 1994).
- Particular professional perspectives, such as nursing and pharmacy (Arthur 1995; Aslani 2000).
- Wider health information (Detmer 2003).

None of this research, however, brings together these separate elements to draw general conclusions about the provision of WMI. This was the aim of the current review.

OBJECTIVES

To assess the effects of providing written information about prescribed and over-the-counter medicines on patient outcomes (knowledge, attitudes, behaviours and health outcomes).

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs in which the effect of written information could be compared with a control group or alternative intervention.

In the protocol we stated that the review would include RCTs in the first instance, with non-randomised controlled trials, controlled before and after studies and interrupted time series studies to be considered in the absence of RCTs. As a number of RCTs were identified for inclusion, we did not extend the selection criterion beyond RCTs, since these provide a more robust level of evidence.

Types of participants

We included trials involving patients of any age who had received written information about a prescribed or over-the-counter medicine, including hospital in-patients and out-patients, or those who received their prescription in primary care. We would also include trials where patients received their medicine from sources other than a pharmacy, such as via the internet, since this increasingly reflects trends in provision. Trials were included regardless of whether or not patients were using a medicine for the first time. We took care to report the context of each trial, particularly in relation to patients included or excluded from participation.

Types of interventions

We included trials of interventions using written information about an individual medicine, such as information contained in a medicine pack insert or a supplementary leaflet intended for the medicine user. We would also include non-print written information about an individual medicine, such as information contained on websites. The (often mandatory) information on dosage and warnings that normally appear on medicine labels were not the focus of the review.

We excluded trials of:

- interventions where medicines information was not the main focus of the intervention,
- information provided that aimed to help a patient choose between two or more medicines,
- information provided to a patient in the form of an individualised illness management plan, and
- information intended to assist doctors or others to prescribe medicines.

We slightly revised the approach we had outlined in the protocol for this review, and instead interpreted 'medicines information' as information fulfilling at least one of the five European Union requirements of mandatory leaflets supplied with medicines (EC 2004).

- What the medicine is and how it works,
- Before taking the medicine (contraindications and precautions),
- How to take the medicine,
- Possible side effects,
- How to store the medicine.

The information might have been given to the patient in isolation, or as one component of a more complex intervention. However, for a trial to be included in the review, it had to be possible to separate the effect of the written information from that of the other intervention(s).

Throughout the review we use the term 'spoken information'. Trials and other publications in this area variously use the terms 'oral information', 'verbal information' and 'spoken information' to describe information communicated other than in a written form.

The term 'verbal information' is potentially confusing because it is used in some WMI research to describe information presented using words (rather than numbers). In the interest of clarity the term 'spoken information' is used throughout this review to describe information communicated other than in a written form, and 'verbal information' to describe the information presented using words (rather than numbers).

Types of outcome measures

We included four types of outcomes relevant to the provision of a written information intervention.

Primary outcomes

A change in patient knowledge about the medicine was the outcome most directly linked to this intervention and was our primary outcome.

Secondary outcomes

The secondary outcomes were:

- changes in patients' attitudes towards taking the medicine (this outcome was added after publication of the protocol),
- changes in patients' medicine-taking behaviour, and
- changes in patients' health outcomes. We anticipated that these were likely to vary considerably according to the setting of the study, and could include physiological indicators (such as change in blood pressure) as well as proxy indicators (such as the number of hospital admissions).

We acknowledge that increased knowledge about the medicine does not automatically mean the patient is more likely to take the medicine; indeed an effect in the opposite direction is possible. The reporting of adverse events was also relevant, given that the WMI might include information on potential side effects of the treatment, and this might have an effect on symptom recognition, classification and reporting by patients.

Search methods for identification of studies

Electronic searches

We searched:

- Cochrane Consumers and Communication Group Specialised Register (January 1970 to June 2007);
- *The Cochrane Library* (2007, issue 1);
- MEDLINE (January 1970 to March 2007);
- EMBASE (January 1970 to March 2007);
- CINAHL (January 1982 to March 2007);
- HMIC (January 1979 to March 2007);
- Index to Theses (January 1970 to January 2007);
- ISI Proceedings (January 1970 to March 2007);
- Pharmline (January 1978 to March 2007);
- Proquest Dissertations and Theses (January 1970 to March 2007);
- PsycINFO (January 1970 to March 2007);
- Sociological Abstracts (January 1970 to March 2007);
- Web of Science (January 1970 to March 2007).

Terms from the strategy developed by the Review Group Trials Search Coordinator for searching the Specialised Register were used as the basis of an MEDLINE (Ovid) search strategy for the review, which was amended following publication of the protocol. Search terms from another review (Forster 2001) were added and a comprehensive search strategy, using a mixture of thesaurus terms and keywords, was developed iteratively in MEDLINE. We scrutinised the results of preliminary searches and the title, abstract and MeSH terms from relevant papers were used to improve the search strategy. We combined the subject search terms with the Cochrane highly sensitive search strategy phases one and two as contained in version 4.2.6 of the Cochrane Handbook (Higgins 2006).
We present the MEDLINE (Ovid) search strategy at Appendix 1; the strategy was adapted for the other databases.
No language restrictions were applied.

Searching other resources

We searched the table of contents (from January 2000 to December 2004) of the following journals:

- International Journal of Pharmacy Practice,
- Patient Education and Counseling,
- The Pharmaceutical Journal,
- Social Science & Medicine,
- Sociology of Health & Illness.

We searched the reference lists from included trials and relevant published reviews to identify further potentially relevant studies. We contacted experts in the field, and publicised the review in appropriate journals and at academic conferences.

Data collection and analysis

Selection of studies

One review author (PS) conducted the search and a second author (DJN) initially screened the studies, by titles and abstracts only for possible inclusion. The full text versions of all possibly-relevant studies not excluded at this stage were independently assessed by two review authors (DJN and PK). Agreement on inclusion of all studies was reached via consensus.

Data extraction and management

Two review authors (DJN and PK) independently extracted data from included studies using a standardised data extraction form, reconciling differences by discussion. We sought missing data and clarification of methods and results from study authors, as well as copies of the written medicines intervention (if it was not published). Data were entered into RevMan by one review author (DJN) and checked by a second review author (PK). When a review author was also author of an included study, the other review author extracted data with a third party.

Studies were combined according to the difference between the interventions compared: specifically trials comparing the effect of WMI against no WMI, and trials comparing the effect of different ways of providing WMI content. We present a structured narrative review of the studies.

We had intended to conduct subgroup analyses looking at preventive and treatment medicines, different population groups and the quality of the information intervention if possible. We had also intended to assess the quality of the WMI intervention using a validated rating scale, if available, and to conduct sensitivity analyses based on the intervention quality. These were not possible due to a lack of comparable studies or data.

Methods of data combination are presented at Appendix 2 for application in a future update of the review, if possible.

When P values were not reported and the raw data were available, a Chi^2 test of association was conducted, using software data available from http://www.quantpsy.org. We used the same method when we aggregated data from studies. For example, in trials with a 2x2 factorial design with four intervention groups where participants received both written information or not, and spoken counselling or not; we aggregated over those receiving spoken counselling or not, for the purpose of the analysis. We then recalculated the P values using the Chi^2 test. Aggregation assumes that there is no interaction between the two variables. In the case of the two relevant trials, in Peveler 1999 no interaction calculation is reported, and in Little 1998 the two variables interact on some of the outcome measures and not on others.

Assessment of methodological quality of included studies

We assessed methodological quality in accordance with the Cochrane Handbook (Higgins 2006). The extent of concealment of randomisation (allocation) was the key methodological quality assessment, since this has been shown to influence the reported size of treatment effect (Schulz 1995) and is likely to be relevant to trials of information provision. We reported whether trials adequately concealed allocation, for example by using third party randomisation. If concealment was not adequate, we noted if the method was inadequate; was not clearly reported; or if randomisation was not concealed.

Another key issue in assessing trial quality, that of masked outcome assessment, was less relevant to this area of research since patient and assessor masking are both difficult to achieve for the provision of written information. We recorded if the outcome assessor was masked.

Consumer participation

The Cochrane Consumers and Communication Review Group's editorial process for the protocol involved two anonymous consumer referees, one from Australia and one from the United Kingdom. A further two consumer referees were included in the editorial process for the full review.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The searches produced 13,613 references, of which 13,466 were excluded by their title or abstract alone. We obtained the remaining 147 papers in full text, of which 122 studies were rejected. For reasons, see Characteristics of excluded studies.

We included trials that compared 'spoken information' alone against 'spoken information combined with written information'. We excluded trials that compared 'no information' with 'written information plus spoken information', because it was not possible to determine the effects of written information alone.

Included studies

We included 25 trials. The trials were conducted in nine countries: eight in the USA; eight in the UK; two in Belgium; two in Canada; and one each in Finland, France, Hong Kong, Switzerland and Turkey. The earliest trial was published in 1972 (Clark 1972), and the most recent in 2004 (Knapp 2004).

Participants

The 25 included trials enrolled 4788 participants; ranging from 34 (Johnson 1986) to 719 (Gibbs 1989). All participants were currently taking a medicine, (an inclusion criterion of this review). The overall mean age of participants, reported in 17 trials, was 43 years (16 to 88 years). In the 20 trials which reported the sex of the participants, 34% were men. Little 1998 enrolled only women (636), as it examined the effects of information about a contraceptive medicine. Excluding Little 1998 the overall proportion of men enrolled in the trials rises to 41%. Two trials reported the

ethnic background of participants (Morris 1982; Vander Stichele 1992). Of the 333 participants in these two trials, 69% were from a non-white ethnic group. However, none of the participants in the trial of Vander Stichele 1992 were from a non-white group. Most trials were poorly reported; the reason participants were offered particular medications could not always be ascertained.

Trial categorisation

We categorised the trials by their experimental intervention and comparison:

1. WMI compared to no WMI: this included trials of WMI versus no intervention, and WMI and spoken information versus spoken information alone.
2. Presentation of WMI: this included trials of WMI versus WMI, and trials comparing ways of providing risk descriptor information.

Information content

The content of the written information provided in the trials was matched to the five content categories of information mandated in the EU (see Background). Eighteen of the 25 trials (72%) published a full or partial copy of the WMI intervention (or later provided one on request), which allowed content analysis. In seven studies, few details of the intervention or its delivery were provided, making problematic the assessment of intervention quality. We noted a considerable amount of heterogeneity in content of the WMI; most interventions, however, included information about 'What this medicine is and what it is used for?' (19 trials); and 'Possible side effects' (19 trials). Six trials provided information pertaining to all five EU categories (Gibbs 1989; Peveler 1999; Regner 1987; van Haecht 1991; Vander Stichele 1992; Vesco 1990).
Ten trials reported a theory or evidence base as the rationale for the design of the intervention. Four trials reported a theoretical basis to their design features and content:

- Bergus 2002 (information-order effect);
- Dodds 1986 (recommendations of *Drugs and Therapeutic Bulletin 1981*);
- Dolinsky 1983 (theory of read-organise-attend); and
- Baker 1991 (*Plain English Campaign* involvement in WMI design, not referenced).

Six trials used evidence-based decision features and content:

- Gibbs 1989 (intervention had been previously piloted, George 1983; Gibbs 1987);
- Desponds 1982 (based on the findings of two research papers, Bellantuono 1980; Greenblatt 1978);
- Labor 1995 (revised after a pilot study, and using Flesch reading levels test (Flesch 1948));
- Arthur 1998 (used Flesch reading levels test, Flesch 1948);
- Strydom 2001a (intervention previously piloted, Strydom 2001b); and
- Clark 1972 (intervention based on results of a questionnaire, not referenced).

Nineteen studies involved WMI for chronic conditions (Arthur 1998; Baker 1991; Bergus 2002; Clark 1972; Gibbs 1989; Johnson 1986; Knapp 2004; Kumana 1988; Little 1998; McBean 1982; Morris 1982: Peveler 1999; Pope 1998; Regner 1987; Robinson 1986; Savas 2001: Strydom 2001a; Vander Stichele 1992; Vesco 1990). This included:

- Five trials that provided information about NSAIDs (Arthur 1998; Gibbs 1989; Pope 1998; Savas 2001; van Haecht 1991); and
- Ten trials that provided information about a cardiovascular medicine (Baker 1991; Clark 1972; Dolinsky 1983; Gibbs 1989; Johnson 1986; Knapp 2004; McBean 1982; Morris 1982; Regner 1987; Vander Stichele 1992).

Five studies provided WMI for acute conditions (Desponds 1982; Dodds 1986; Labor 1995; Peura 1993; van Haecht 1991); and one for both chronic and acute conditions (Dolinsky 1983).
Four trials provided information about a medicine for treating mental health problems (Desponds 1982; Peveler 1999; Robinson 1986; Strydom 2001a) and three for antibiotics (Dodds 1986; Dolinsky 1983; Peura 1993). Four trials provided information about medicines not within these classes (Bergus 2002; Kumana 1988; Labor 1995; Little 1998). Five trials (Dolinsky 1983; Gibbs 1989; Johnson 1986; McBean 1982; Vander Stichele 1992) provided information for more than one medicine.
Eleven studies involved WMI for multiple medications (Arthur 1998; Baker 1991; Desponds 1982; Dodds 1986; Dolinsky 1983; Dolinsky 1983; Knapp 2004; Peura 1993; Peveler 1999; Strydom 2001a; Vander Stichele 1992) and 13 studies involved WMI for single medications (Bergus 2002; Clark 1972; Johnson 1986; Kumana 1988; Labor 1995; Little 1998; McBean 1982; Morris 1982: Pope 1998; Regner 1987; Savas 2001: van Haecht 1991; Vesco 1990). In one study the number of medications was unclear although it appeared to be for multiple medications for treating mental health problems (Robinson 1986).

Risk of bias in included studies

Many included studies did not report clearly how they were conducted, making it difficult to assess their quality. Ten trials reported adequate randomisation (Arthur 1998; Bergus 2002; Knapp 2004; Little 1998; Peveler 1999; Pope 1998; Savas 2001; Strydom 2001a; van Haecht 1991; Vander Stichele 1992), while 15 trials either failed to report their randomisation method, or reported it in an unclear manner.
Eight trials reported how they attempted to conceal allocation, but only five of these (Arthur 1998; Desponds 1982; Little 1998; Peveler 1999; Strydom 2001a) were judged to have done so adequately (using either remote access or coded/numbered envelopes). Therefore the other three trials (Johnson 1986; Knapp 2004; Pope

1998) were judged to have inadequately concealed the allocation process. The remaining 17 trials did not clearly report how they had concealed allocation.

Ten trials described an adequate method for blinding the outcome assessment (Desponds 1982; Johnson 1986; Kumana 1988; Labor 1995; Little 1998; McBean 1982; Peveler 1999; Pope 1998; Strydom 2001a; van Haecht 1991); two trials reported a method which was inadequate (Dodds 1986; Knapp 2004).

Twenty two trials reported loss to follow-up (Arthur 1998; Baker 1991; Clark 1972; Desponds 1982; Dodds 1986; Dolinsky 1983; Knapp 2004; Kumana 1988; Labor 1995; Little 1998; McBean 1982; Morris 1982; Peura 1993; Peveler 1999; Pope 1998; Regner 1987; Robinson 1986; Savas 2001; Strydom 2001a; van Haecht 1991; Vander Stichele 1992; Vesco 1990). This ranged from none (Desponds 1982; Dolinsky 1983; Knapp 2004) to 68% (Robinson 1986). Mean loss to follow-up in the 22 trials reporting it was 16%. Loss to follow-up is defined as outcome measurement being unavailable or incomplete at the final data collection for each trial.

Eleven trials clearly reported when participants withdrew (Arthur 1998; Clark 1972; Desponds 1982; Dodds 1986; Dolinsky 1983; Knapp 2004; Labor 1995; Savas 2001; Strydom 2001a; Vander Stichele 1992; Vesco 1990). Withdrawal rates ranged from none (Clark 1972; Desponds 1982; Dolinsky 1983; Knapp 2004) to 37% (Labor 1995). Mean withdrawal in these eleven trials was 12%. Withdrawal is defined as non-receipt or partial non-receipt of the intervention after randomised allocation.

Effects of interventions

Outcome data are presented in Table 1.

There was extensive heterogeneity in the design and conduct of the 25 included trials, and the outcomes measured; therefore a statistical synthesis was not possible. Measures of knowledge and satisfaction were often developed for individual trials and appeared to measure different components of these outcomes. Some studies reported few details of the intervention or its delivery, making problematic an assessment of intervention quality. We present a structured narrative and tabular review of the study results.

Twenty trials compared WMI to no WMI, and eight trials compared different types of WMI presentation.

No studies showed an adverse effect from WMI.

Written medicine information versus no written medicine information

Twenty trials compared the effect of providing WMI with no WMI (Arthur 1998; Baker 1991; Clark 1972; Dodds 1986; Dolinsky 1983; Gibbs 1989; Johnson 1986; Kumana 1988; Little 1998; McBean 1982; Morris 1982; Peura 1993; Peveler 1999; Pope 1998; Regner 1987; Robinson 1986; Savas 2001; Strydom 2001a; Vander Stichele 1992; Vesco 1990). Little 1998 compared two different WMI interventions with a blank leaflet. Clark 1972 and Dolinsky 1983 each compared the effects of two different WMI interventions with no written or spoken information. We report the comparison of the two WMI formats for each of these three studies (Clark 1972; Dolinsky 1983; Little 1998) below.

Of the 20 trials comparing the effect of providing WMI with no WMI, 12 trials compared WMI against no information (Clark 1972; Dodds 1986; Dolinsky 1983; Gibbs 1989; Johnson 1986; Kumana 1988; Little 1998; McBean 1982; Morris 1982; Peveler 1999; Vander Stichele 1992; Vesco 1990). The other eight trials gave both groups in the trial (those receiving and those not receiving WMI), additional spoken information (Arthur 1998; Baker 1991; Peura 1993; Pope 1998; Regner 1987; Robinson 1986; Savas 2001; Strydom 2001a).

Seventeen of the 20 trials in this broad category measured a change in knowledge (Arthur 1998; Baker 1991; Clark 1972; Dodds 1986; Dolinsky 1983; Gibbs 1989; Johnson 1986; Kumana 1988; Little 1998; McBean 1982; Morris 1982; Peura 1993; Pope 1998; Regner 1987; Robinson 1986; Savas 2001; Strydom 2001a); three a change in attitudes (Baker 1991; Gibbs 1989; McBean 1982); and eight a behavioural outcome (Dodds 1986; Dolinsky 1983; McBean 1982; Morris 1982; Peveler 1999; Robinson 1986; Vander Stichele 1992; Vesco 1990). Seven trials (Baker 1991; Dodds 1986; Dolinsky 1983; Gibbs 1989; McBean 1982; Morris 1982; Robinson 1986) measured more than one type of outcome.

No trials measured a health outcome.

Knowledge

Most of the studies measuring knowledge did so in a way that was unique to that trial (see table Characteristics of included studies). Findings were mixed, although most studies measuring knowledge found that either the WMI intervention increased knowledge, including recall of the information and recall of side effects, or made no difference. Twelve trials examined the effect of WMI compared to no information on knowledge: six found a statistically significant effect favouring WMI (Arthur 1998; Clark 1972; Johnson 1986; Little 1998; Robinson 1986; Savas 2001); three trials (Kumana 1988; McBean 1982; Strydom 2001a) did not. The three remaining trials (Dolinsky 1983; Gibbs 1989; Pope 1998) found a mixture of significant and non significant results. In the trial by Gibbs 1989, more participants receiving written information gave the correct answer to questions about the medicine, for four of nine questions. Significantly more people who received no WMI knew the name of the medicine compared to those who received WMI. (These results were statistically significant). Participants receiving WMI had significantly greater awareness of side effects (aggregated over all study drugs) than those receiving nothing. In the trial by Pope 1998, two of 11 knowledge outcomes were statistically significant: one favouring the written information, and one favouring the control. The trial by Dolinsky 1983 reported no significant difference in correct recognition of the two study drugs between those given one of two WMI interventions

and those receiving no intervention, but did not report individual statistical comparisons between groups.

We further sub-categorised the trials measuring knowledge according to the particular types of knowledge they assessed.

Recall of information about the medicine

Four trials examined participants' recall of the information they were given about the medicine (Baker 1991; Dodds 1986; Little 1998; Peura 1993). The trial by Dodds 1986 found significantly higher recall among those given WMI compared with those who were not. Two studies found a significant difference for only half of the questions asked (Baker 1991; Peura 1993). Little 1998 used a factorial design to compare the effectiveness of an experimental evidence-based summary leaflet, a standard leaflet and no leaflet, on women's knowledge of an oral contraceptive. This was in addition to an assessment of the effect of questioning by their doctor or nurse. Outcomes (measured by a validated questionnaire) were aggregated by whether or not the participants were questioned. The trial reported that recall was greater for patients given the 'summary leaflet' (33%) than those given no WMI (19%), ($P < 0.05$). However, patients given the full Family Planning Association leaflet did not have better recall than the no WMI group.

Recall of side effects

Six trials measured knowledge about side effects (Baker 1991; Gibbs 1989; Morris 1982; Peura 1993; Pope 1998; Regner 1987). Four of these trials found that patients given WMI had higher knowledge of side effects compared with those given no WMI; these results were statistically significant in three trials (Baker 1991; Peura 1993; Regner 1987). Morris 1982 found that the group given WMI were able to name more side effects at follow-up, but also named more incorrect side effects than the control group. Tests for statistical significant were not reported by this study, and there was not enough data reported to calculate P value. In contrast, Pope 1998 found that patients given the information sheet/leaflet listed fewer side effects ($P = 0.02$), although the number of correct side effects listed was not statistically significant between the two groups ($P = 0.09$).

Attitudes

Three trials comparing the provision of WMI with no WMI assessed participants' attitudes towards the information given; specifically whether or not they felt satisfied with the information provided (Baker 1991; Gibbs 1989; McBean 1982).

Baker 1991 examined participants' attitudes regarding the usefulness and ease of comprehension of the WMI (both groups received spoken information, with one group receiving additional WMI). Significantly more participants receiving the WMI felt it was easy to understand (84%) compared with those receiving only spoken information (33%). There was also a significant difference in perceptions of the information's usefulness: 84% receiving WMI thought it was useful or extremely useful, compared with 33% of those in the control group ($P < 0.001$). Additionally, significantly more people receiving WMI felt that they had been given sufficient information (74%) compared with those in the control group (14%; $P < 0.001$).

Baker 1991 also examined whether the provision of WMI in addition to spoken information reduced worry about drug treatment, and found a statistically significant effect: 53% of those given additional WMI reported less worry, compared to 25% in the control group ($P < 0.05$). Participants given no WMI were more likely to feel that information about medicines given to them could be improved: 64% compared with 27% among those who had been given WMI ($P < 0.001$). Similarly Gibbs 1989 and McBean 1982 reported that participants given WMI expressed greater satisfaction with the information provided. This difference was statistically significant in the trial by Gibbs 1989. McBean 1982 did not test for significance.

Behaviour

Eight trials assessed the effects on behaviour of providing WMI versus not providing WMI (Dodds 1986; Dolinsky 1983; McBean 1982; Morris 1982; Peveler 1999; Robinson 1986; Vander Stichele 1992; Vesco 1990). Six trials examined compliance with the medicines' instructions: compliance was found to be higher among people given WMI. However no difference was found when biological markers were used to assess compliance. Three studies found that compliance was greater for those who had received WMI (Dodds 1986; McBean 1982; Robinson 1986), although one of these studies did not report statistical tests (McBean 1982). There was no difference in compliance between the groups in one trial (Vander Stichele 1992). McBean 1982 and Dodds 1986 performed a tablet count; but Dodds 1986 also interviewed patients. Vander Stichele 1992 used a monitored dose system; while Robinson 1986 measured compliance as rated by the psychiatrists (based on a combination of patient report; tablet count; and clinical judgement).

Morris 1982 examined the mean number of health problems reported by participants. They found that the group given WMI reported on average slightly more side effects at follow-up: 4.1 out of a possible 17, compared to 3.6 out of 17 for the control group. Tests for statistical significant were not reported by this study, and there was not enough data reported to calculate a P value. In the trial by Peveler 1999 we aggregated the effect of information against none by combining the groups receiving counseling or no counseling. No difference was found in the self-reported continuation of the medication for those receiving written information, and those receiving none. Vesco 1990 confirmed compliance - or adherence to the treatment regime - through assayed blood levels,

and found no difference between those given WMI and those not given it, although this result was not significant. The study also found no significant differences between intervention and control groups in the proportion who stopped taking their medication, but did find that significantly more people in the WMI group reported a side effect (P < 0.05).

The trial by Dolinsky 1983 reported no significant difference in correct application of information about the two study drugs between those given one of two WMI interventions and those receiving no intervention, but did not report individual statistical comparisons between groups.

Written medicine information presentation

Eight trials compared the effects of presenting WMI in different ways (Bergus 2002; Clark 1972; Desponds 1982; Dolinsky 1983; Knapp 2004; Labor 1995; Little 1998; van Haecht 1991). Five of these trials measured knowledge (Clark 1972; Desponds 1982; Dolinsky 1983; Knapp 2004; Little 1998), four an attitudinal outcome (Bergus 2002; Desponds 1982; Knapp 2004; Labor 1995), and two behaviour change (Dolinsky 1983; van Haecht 1991). We found no trials measuring a health outcome.

Knowledge

The majority of the five trials comparing different ways of presenting WMI used heterogeneous outcomes to measure 'knowledge'. Findings were mixed, although most studies found the intervention either improved knowledge or made no significant difference.

Clark 1972 found that programmed instruction significantly increased understanding of the use of the drug, compared with the standard format handout (P = 0.008).

Desponds 1982 also used a factorial design to compare the effect of an experimental leaflet with the manufacturer's leaflet, for each of four anxiety medications. More participants given the experimental leaflet answered the questions correctly (47%), compared to those receiving the manufacturers' leaflet (38%), but no statistical tests were performed to determine whether the result was significant.

Dolinsky 1983 found no significant difference in correct recognition of the two study drugs between those given WMI in a 'read-organise-attend' format or those given an easy-to-read format ('readable' information) or those given no intervention, but individual statistical comparisons between groups were not reported.

Knapp 2004 found that providing information of the risk of side effects as a numerical description was significantly more effective in helping people make a correct estimation of risk than giving the same information as a written verbal description (see Table 1).

Little 1998 found more women who were given the evidence-based summary leaflet correctly answered all questions (33%) compared with those given the standard leaflet (24%), but this difference was not statistically significant.

Attitudes

Four trials comparing different ways of presenting WMI measured attitudinal outcomes (Bergus 2002; Desponds 1982; Knapp 2004; Labor 1995). The findings showed the experimental WMI had a significant effect on attitude, although these outcomes varied between trials.

Two trials (Bergus 2002; Knapp 2004) examined whether presenting the WMI in different ways affected participants' decisions to take the medicine. Bergus 2002 found that the order in which people were given information about the benefits of a medication and the likelihood of side effects affected ratings of favourability of treatment; they were significantly less favourable when information about the risks was given after information about the benefits (P = 0.02). Knapp 2004 examined participants' satisfaction with side effects risk descriptor information, which was provided numerically or verbally. People who had read the verbal information were more likely to say it would have an effect on their decision to take the medicine, and this difference was statistically significant for one of two side effects (constipation; P < 0.05).

Knapp 2004 also found that people who received numerical risk information reported being more satisfied with the information than those receiving verbal information; this difference was statistically significant for one of two side effects (pancreatitis; P < 0.05).

Labor 1995 examined the effect of five leaflets that varied in terms of wording and the amount of information included. Significantly more participants given WMI with 'normal' wording judged the length to be 'about right' (P < 0.0001) and the complexity to be 'about right' (P < 0.0001), compared with those given other formats. Participants given information worded for professionals were more critical of it than those who received simple or normally worded information (P = 0.24). Participants given simply worded information judged it to be more useful than any other group (P = 0.19).

Desponds 1982 found that participants receiving the experimental information more often reported feeling the text to be easy to understand (P < 0.01), complete (P < 0.05) and to have a lot of new information (P < 0.05). The differences between participants' views of the experimental and standard information on being 'easy to read' or 'interesting' were not statistically significant.

Behaviour

Two trials examined aspects of behaviour, and neither found a significant effect of one WMI over another. Dolinsky 1983 found no significant difference in the correct application of the two study drugs between those given WMI in a 'read-organise-attend' format or those given an easy-to-read format ('readable' information) or those given no intervention, but individual statistical comparisons between groups were not reported. van Haecht 1991 found no statistical difference in the proportion of people that reported reading a leaflet thoroughly when an experimental leaflet with improved

readability and layout was compared with a traditional insert (P = 0.15).

DISCUSSION

Summary of main results

Most of the 25 studies included in this review did not report their methods clearly; and where reporting was transparent, we often judged that the studies had not been conducted in such a way as to reduce bias. Several studies did not conduct statistical tests on the study results, and there was considerable heterogeneity in terms of the types of WMI interventions used and the outcomes measured. These are not necessarily barriers to meta-analysis as some heterogeneity between interventions is inevitable. The heterogeneity of outcome measures was large however, which negated the possibility of a meta-analysis. We could not combine the results of trials to determine if WMI was effective in changing knowledge, attitudes or behaviour related to medicine taking. Furthermore, a number of recent trials were not included in this review because they assessed condition-based information, rather than medicines-based information, and therefore did not meet the inclusion criteria. We found no trials that evaluated the effects of WMI on health outcomes. Despite systematic searching, we were not able to identify relevant trials published later than 2004 for inclusion. We would welcome information on trials that we may have inadvertently missed.

Some individual trials showed improved knowledge about a medicine for people receiving WMI compared to those who did not. For example, the trials measuring recall of information (Baker 1991; Dodds 1986; Little 1998; Peura 1993) tended to favour the provision of written information, as did those measuring recall of side effects (Baker 1991; Gibbs 1989; Morris 1982; Peura 1993; Pope 1998; Regner 1987). In around half of the trials these results were statistically significant.

To determine whether one way of presenting WMI was more effective than another, we evaluated trials that compared different ways of presenting information. Again the evidence was inconclusive. One trial examining understanding of the risk of side effects found that written information provided numerically was significantly more effective than written information provided verbally (Knapp 2004). This is consistent with the findings of a series of trials that evaluated risk descriptor information in hypothetical scenarios using homogenous interventions and outcome measures (for example Berry 2002a; Berry 2004). These trials were not eligible for inclusion in this review, but were included in the UK Health Technology Assessment (HTA) report (Raynor 2007b), which found, contrary to EU guidance, that giving information about the risk of a side effect as a numerical descriptor was more effective than a verbal risk descriptor for improving people's understanding of the risk.

Knapp 2004 also found that providing information about the risk of a side effect numerically can significantly affect people's attitudes to taking a medicine. However, the overall evidence of the impact of WMI on attitudes was unclear. In addition, the general difficulty in quantifying an attitude (Littlewood 2005) can cast some doubt on the validity of several trials which used this as an outcome measure.

Five of the six trials measuring compliance found that the provision of WMI helped to achieve compliance, but the results were significant for only two trials (Dodds 1986; Robinson 1986). Dodds 1986 relied on self-reported compliance with antibiotic treatment over three to five days. Robinson 1986 measured follow-up of unnamed drugs for treating mental health problems for a fortnight only. It is debatable whether these findings of compliance relating to short-term medicine use can be generalised to more chronic conditions. Overall there was no strong evidence that providing WMI on its own will improve adherence to medicine instructions. Furthermore, it is important to recognise that an informed decision may lead someone *not* to take a medicine (Raynor 2007b).

We hoped to examine the effects of internet-based medicines information, but found no trials evaluating this form of WMI. Users of medicines have expressed the need for evaluation of internet-based medicines information (Raynor 2007b) and the lack of studies of WMI provided on the internet identifies a gap between the themes examined in reviews of medicines information and the needs of users (Nicolson 2006). This evidence gap highlights the need to put the evaluation of internet-based medicines information firmly on the research agenda (Nicolson 2007).

Overall completeness and applicability of evidence

Because of the large degree of heterogeneity in the design of the interventions, the outcomes chosen and the way the outcomes were measured, we were unable to perform a meta-analysis. For example, comparing the WMI to the EU categorization, we noted wide differences in the specific content presented. This examination was further hampered by a number of papers not providing a copy of the intervention, or not adequately describing the intervention. The outcomes measured differed widely, and when trials reported the same outcome (e.g. knowledge), this was often done using a trial-specific tool. In addition to these problems, we found several trials lacked statistical tests, and provided insufficient information to enable us to perform these. Our inability to conduct a meta-analysis meant that we were unable to undertake sub-group analyses, or test for heterogeneity of the results. Future trials should use common outcomes (perhaps using standardised measures), so as to enable a quantitative synthesis. Furthermore the evaluation of interventions containing medicines information under standard headings or criteria would also enable a quantitative synthesis.

The overall mean age of the participants in the trials reporting age was 43 years, yet most people who take medicines long-term, and so perhaps have the greatest need for effective information, will be older. This suggests that study participants may not be representative of the target audience of WMI.

Some older trials in the review, particularly those comparing WMI with no WMI, might be seen as less relevant in the context of current health care. Patients can now access information about medicines and other aspects of health care on the internet, and so trials including comparison groups given no WMI are likely to be less convincing. The evaluation of WMI by trials therefore necessarily reflects the regulatory context that determines its provision. For example, in the USA, Japan, Australia, Israel, and in the EU, there are specific laws that govern the use of WMI. This presents a challenge for research: EU legislation means that research evaluating the effects of WMI compared with no WMI is no longer possible. Instead research compares the impact of presenting WMI in different formats, to evaluate their relative effectiveness. Future versions of this review will contain more trials comparing the effect of two or more formats of WMI, and it is likely that the number of included trials examining the relative effect of WMI will eventually outnumber the trials examining the absolute effect (i.e. WMI vs. nothing).

We also found it rare for information in the included trials to be provided in accordance with all five EU medicines information categories; only six trials provided information reflecting all five categories. The evidence has therefore largely been derived from trials examining interventions that do not reflect current standards for WMI (in the EU); for example most trials did not provide information relevant to 'before taking the medicine' or 'how to store it'. This can again be considered an historical effect, as many of the trials were conducted before this legislation was enacted.

Enabling medicine users to be involved in making an informed choice about taking their medicines is a fundamental principle of concordance (also known as 'partnership in medicine taking'), and promoted in policy documents across many countries; for example in the EU by EC 1992. It is disappointing then that there is no clear evidence to show the effectiveness of WMI for changing knowledge, attitudes and behaviours relating to medicine taking.

Quality of the evidence

The conduct of the trials as a whole was poor, and this casts doubt on their results. For example only ten trials confirmed adequate blinding of the outcome assessor. Furthermore, at least three trials inadequately concealed the allocation sequence (and a further 17 trials did not report how this was conducted). Inadequate concealment is the greatest source of overestimation of treatment effects (Juni 2001), therefore doubt may be cast on the validity of the results of these trials.

The poor quality of many of the included trials has limited our capacity to provide a conclusive answer to the research question. One explanation is that this represents an historical effect, as most studies were conducted before the CONSORT statement, when there was less consensus on what constituted best practice in trial conduct.

Agreements and disagreements with other studies or reviews

There are few systematic reviews relevant to the area of medicine information for consumers, with which to compare our findings. Haynes 2008 evaluated interventions to help patients follow prescriptions for medicines. Of the 78 trials they included, 18 examined the provision of verbal, written, or visual material for patients. Of these, we included one which met our inclusion criteria: Peveler 1999. Haynes 2008 was able to distinguish between the short-term and long-term effectiveness of different methods to improve adherence to medications; whereas we were unable to determine if written information is effective per se.

Our review is one component of a wider review of the role, value and effectiveness of WMI (Raynor 2007b). This review found medicine users do not value WMI as it is currently provided, and a key element in providing effective WMI is the application of the principles of plain writing and information design. Leaflets that are well written and designed, with a sound theoretical basis for their wording and design, stand a better chance of getting their message across effectively. Research is needed to determine how far information derived from these principles affects knowledge and attitudes. To date this has been the exception rather than the norm; more than half the trials included in our review had no explicit theoretical or evidence base for the design and content of the medicines information. Essentially these studies examined a stimulus-response relationship; they can show an association, but cannot explain why the design of the information was effective or not. The importance of appropriate wording and design of WMI is acknowledged by European legislation which stipulated that from 2005 medicines information had to be tested on target groups to ensure legibility, clarity, and ease-of-use (EC 2001). This paved the way for the usability testing of all medicine information leaflets (EC 2004), which affects the design and provision of WMI, as well as how subsequent research will evaluate WMI.

AUTHORS' CONCLUSIONS

Implications for practice

WMI should be available, not only because of legislation, but because this review has found evidence, albeit from poorly conducted studies, to show that it may improve knowledge of the medicine. Furthermore, no studies showed an adverse effect from WMI.

Implications for research

The review identified the need for research to assess the links between information provision, behaviour, and health outcomes. We included trials which measured a behavioural outcome, for example complying with the instructions for taking the medicine, because it is important to know whether people are taking prescribed medications as directed. However, the use of behavioural change as an outcome measure of the effectiveness of written information about medicines can be doubted. We say this for two reasons. First, the relationship between medicines information and behaviour is probably far from direct, with many potential intervening variables. Second, some of the outcomes measured may not be relevant to people taking medicines; compliance is an example, which reflects the goals of those prescribing the medicines and not necessarily the goals of those taking them. Similarly, drawing a possible link between WMI and health outcomes may be difficult to assess because of the indirect relationship, and numerous extraneous variables to be considered. Still, an aim of information provision is to improve health outcomes, albeit modified by knowledge, attitudes and behaviours. Therefore there is a need for well-designed research to examine this relationship.

Other research implications are as follows.

- First, future trials examining the effectiveness of WMI should use consistent and validated outcome measures to enable statistical comparison between studies.

- Second, future trials need to apply recognised standards to their design, conduct and reporting.

- Third it may be worthwhile to define and apply an optimal length of follow-up to evaluate the effectiveness of WMI over the longer term. This is particularly important for medicines used for chronic conditions.

- Fourth, there is a need for research to evaluate the effect of applying best practice in the design of the leaflet on knowledge and attitudes. In particular, there is a need to examine how understandable the information in the leaflets actually is to users.

- Fifth, trials will benefit from greater input from qualitative research, to help examine the role of WMI and the value that people place on it.

- Finally, more research to evaluate internet-based medicines information is needed.

ACKNOWLEDGEMENTS

For translation of papers that were not written in English, we thank Pierre-Olivier D'Amours for translation of Desponds 1982 and Mirjam Harmsen for translation of Pander Maat 1996, (which was excluded upon reading the translated version). We thank France Légaré for putting us in contact with Pierre-Olivier. We thank Jeremy Henley and Anne Forster for their involvement in devising the initial protocol for this review in 2000; and Alison Blenkinsopp, Janet Grime, Kristian Pollock, Simon Gilbody, John Maule, Gill Dorer, and David Dickinson for their involvement in revising the protocol for this review in 2004. We thank the reviewers for their feedback on drafts of this review, and the editors and staff of the Cochrane Consumers and Communication Review Group, particularly Drs. Sophie Hill, Dell Horey and Megan Prictor.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Arthur 1998

Methods	Randomisation method: adequate (computer generated) Concealment of allocation by remote access. Baseline comparability: not reported. Blinding: not reported. 8 to 12 weeks follow-up.
Participants	UK. 80 adult patients (mean age 53 years; range 20 to 88) who had been prescribed or were already taking one of six NSAIDs. 27% were male. They were excluded if their sight was impaired, they were unable to read English, or if they had a history of inflammatory joint disease for more than five years
Interventions	Intervention group: given patient information leaflet, and spoken explanation. The leaflet design and content was based on evidence of readability, text size and style of layout (coloured card) Control group: No written information provided, but received the spoken explanation alone which was the same as the information in the leaflet. Leaflet was given at the end of the study The information was for one of six NSAID (Non-Steroidal Anti Inflammatory Drugs); trade (generic) names: Naprosyn (naproscen); Indocid (indomethacin); Brufen (ibuprofen); Relifex (nabumetone); Oruvail (ketoprofen); and Voltarol (diclofenac). This is used for treating inflammation of the joints, a chronic condition. The information was on the nature of inflammatory joint disease, explanation of NSAID drug, how drug works and should be taken, its administration in relation to most common side effects, side effects themselves, the drug and pregnancy, and safe storage of the drug. Spoken information was on name of NSAID, description on how to take the drug, its effects, side effects and to contact doctor in such an event Copy of leaflet available. Leaflet was written in English language. Information was provided by the author.
Outcomes	Knowledge: number who correctly identified the six drugs as NSAIDs
Notes	A third group received the leaflet only. This was not extracted as it would not isolate the effect of WMI Additional demographic data, results for the individual groups, and information about concealment of allocation were supplied by the author Total withdrawal: 6/80 (8%) Total loss to follow-up: 6/80 (8%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Baker 1991

Methods	Randomisation method: not reported. Baseline comparability: for age and sex. Blinding: not reported. 2 weeks follow-up.
Participants	UK. 125 adults (mean age 52 years) who were admitted to a Regional Cardiology Unit and were able to read English. 63% were male. They were excluded if they were taking drugs for which there was no leaflet
Interventions	Intervention group: patient information wallet comprising: (i) Introductory leaflet giving general advice about the drug treatment; the importance of taking each dose as stated; seeking specific advice if pregnant; driving as usual; drinking in moderation; destroying drugs not needed and asking if more information is needed. (ii) Leaflets on specific prescribed individual drug stating what it does, precautions, and other information. Spoken information also provided about the drug Control group: No written information provided; spoken information only The information was for 1 of 16 drugs covering four groups: glyceril trinitrate sublinguinal (GTS) tablets; beta-blockers; warfarin; and digoxin; used for treating a cardiovascular (heart) condition, that is chronic. The generic names of the drugs were: angiotensin converting enzyme inhibitators; amiodarone; beta-androceptor antagonists; digoxin; diltiazem; dipyridamole; glyceril trinitrate; loop diruetics; nifedipine; oral nitrates; potassium supplements; spironolactone; thiazide diruetics; verapamil; warfarin. Provider of WMI not reported. Copy of WMI available. English language WMI. Theory based - "Plain English Campaign" involved in WMI design
Outcomes	Knowledge: recall information before leaving hospital to answer a number of questions about taking drug (s): treatment purpose; action if miss dose; possible side effects; action re side effects; when to take drug; how to take drug; whether you can drive; whether you can drink alcohol Attitudinal: sufficient information felt to have been given; information felt to be clear and easy to understand; information felt to be useful or extremely useful; reduced worry about drug treatment as a result of specific information; felt information could be improved
Notes	Total withdrawal: not reported Total loss to follow-up: 24/125 (19%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Bergus 2002

Methods	Randomisation method: adequate (random number table) Baseline comparability: for sex, age and stroke familiarity. Blinding: not reported. Follow-up length unclear.
Participants	USA. 217 adult patients (mean 39 years; range 18 to 70). 35% male. Excluded if non-English speaking

Bergus 2002 (*Continued*)

Interventions	Intervention group one: brochure with information about risks followed by benefits Intervention group two: brochure with information about benefits followed by risks No further spoken information was provided. Included information was: risk of stroke = 2% over three years, reduced to 1% by use of aspirin. Risk of GI side effects 40% with aspirin, two-fold increased risk of ulcers (but < 1/1,000 per year). Risk of intracerebral haemorrhage 1/3,000 per year which is half that of non-aspirin users The information was for aspirin, a generic drug with no trade name, used to decrease the risk of stroke in carotid artery stenosis, a chronic condition. Copy of WMI available. English language WMI. Theory based (information-order effect).
Outcomes	Attitudinal: change in favourability of treatment rating
Notes	Participants were also randomised to two surgical treatments for symptomatic carotid stenosis. These were not extracted as they do not isolate the effect of WMI Total withdrawal: not reported Total loss to follow-up: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Clark 1972

Methods	Randomisation method: not reported. Baseline comparability: not reported. Blinding: not reported. 1 to 3 days follow-up.
Participants	USA. 45 adults (range 21 to 77 years) attending anticoagulant therapy clinic. 49% were male. Participants had spent on average 11 years in education. Discharged on warfarin therapy. Included if they could understand English and were able to distinguish small print
Interventions	Intervention group one: "Programmed Instruction" booklet divided into five sections: action and indication for use of drug; laboratory testing; calculation of dosage; factors altering effect of drug; safety factors. Provider of WMI not reported Intervention group two: two page handout information sheet containing same essential information as the programmed instruction booklet. Provider of WMI not reported Control group: No written or spoken information provided. The information was for warfarin, an anticoagulant (class of drug) used to thin blood. This is for the treatment of a chronic condition. The generic and trade names for this drug were not reported. Copy of partial WMI available. Written in English. Evidence based: content based on questionnaire results

Clark 1972 (*Continued*)

Outcomes	Knowledge: understanding of the use of the drug (possible score is 15)
Notes	The information was for an anitcoagulant, warfarin. Total withdrawal: 0/45 (0%) Total loss to follow-up: 1/45 (2%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Desponds 1982

Methods	Randomisation method: not reported. Concealment of allocation by coded envelope. Baseline comparability: for age, sex, first language, and education. Outcome assessor only blinded. 2 to 3 day follow-up.
Participants	Switzerland. 268 hospitalised adult patients (mean 60 years); 76% had previously received one of four benzodiazepines (bromazepam, oxazepam, nitrazepam, flunitrazepam). 43% male. 86% French first language; 18% had previously received spoken information about the drug; 59% had previously read the Patient Information Leaflet (PIL); 92% considered the PIL important. Participants were excluded if they had psychiatric or visual problems
Interventions	Intervention received standardised WMI: the experimental PIL. Had more text than manufacturer PIL, which was less medical. Included precaution and secondary effects, including addiction Control received manufacturer WMI: more information on the therapeutic effect. No mention of action to take in the event of accidental overdose or that the medicine required a prescription The information was for one of four benzodiazepine drugs (generic names) bromazepam, oxazepam, nitrazepam, flunitrazepam, used to relieve agitation, normally an acute condition
Outcomes	Attitudinal: Felt text: easy to understand; easy to read; interesting; judged to be complete; a lot of new information. Knowledge: Aggregated % all correct, % partly correct, % missing, % wrong for questions about four drugs
Notes	It is not clear from the reporting of the paper if additional spoken information was given or not. It is possible that this was given, but it was not formally linked to the WMI provided Total withdrawal: 0/222 (0%) Total loss to follow-up: 0/222 (0%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Desponds 1982 (*Continued*)

Allocation concealment?	Low risk	A - Adequate

Dodds 1986

Methods	Randomisation method: not reported. Baseline comparability: for age, sex, drugs prescribed. Blinding: only one of two outcome assessors blinded, hence consider to have been inadequate. 3 to 5 day follow-up.
Participants	UK. 68 adults (mean age 28 years; range 16 to 81) discharged from hospital. 23% male. Included if discharge prescription included up to four drugs and more than one antibiotic (more than five days) to be self-administered
Interventions	Intervention group: One of seven WMI on how to take drug, storage, what to do if miss dose, how it is expected to help condition, and how to recognise side effects. A5 folded leaflet on coloured paper. Poorly understood words and phrases were avoided. Readability and suitability of the WMI was assessed. Expert consultation on layout of information. Question and answer format used to avoid the WMI appearing dictatorial. Pictures used. Provider of WMI not reported Control group: No written information provided. The information was for one of eleven antibiotics (ampicillin, amoxycillin, cephalosporins, co-trimoxazole, erythromicin, flucloxacillin, Magnapen, metronidazole, penicillin V, tertracycline, trimethropin), used to treat bacterial infections, an acute condition. These are all generic drug names except Magnapen, which is a trade name as it contains two antibiotics. Copy of WMI available. Theory-based. English language
Outcomes	Knowledge: median recall of information essential to correct drug taking Behaviour: median patient behaviour questionnaire score for assessing actual drug taking Behaviour: median patient compliance score (measured by tablet count and interview)
Notes	If 'counselling' about their medicines was requested, patients were withdrawn from the study. The prescriber instructions were written, not spoken. Total withdrawal: 5/68 (7%) Total loss to follow-up: 7/68 (10%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Dolinsky 1983

Methods	Randomisation method: not reported. Baseline comparability: not reported. Blinding: not reported. Length of follow-up unclear.
Participants	USA. 271 adults in receipt of prescription for either study drug from one of four outpatient clinics, one community pharmacy, or one clinic, from a range of educational and occupational backgrounds
Interventions	Intervention group 1: WMI sheet providing information on how to take the medicine, in the read-organise-attend format, using underlining and shorter paragraphs than intervention group 2. Provider of WMI not reported Intervention group 2: WMI sheet with the same information as above, in the easy-to-read format, using information that was 'readable'. Provider of WMI not reported Control group: No written or spoken information provided. The information was for a drug (generic name) methyldopa, used to treat high blood pressure, (a chronic condition); or a drug (generic name) ampicillin, used to treat bacterial infections (an acute condition). Copy of WMI available. English language. Theory based.
Outcomes	Knowledge: correct recognition of drug information for either study drug. Behaviour: correct application of drug information for either study drug
Notes	This may have been a one day trial, which would change our judgement of numbers lost to follow-up and withdrawal, but we could not ascertain this Total withdrawal: 0/271 (0%) Total loss to follow-up: 0/271 (0%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Gibbs 1989

Methods	Randomisation method: Cluster randomisation of four towns. Baseline comparability: for age and sex. Blinding: not reported. 12 weeks follow-up.
Participants	UK. 719 adults (over 16 years). 36% male from a small town attending a GP surgery and currently prescribed one of the study drugs
Interventions	Intervention: two sided WMI based on evidence. On the front was a short summary and on the back greater detail was provided explaining the actions of the drug; what to do before, when and after taking the drug; and storage of the drug. Cartoon icons were used. WMI was issued by GP during consultation or by pharmacist during dispensing

Gibbs 1989 (*Continued*)

	Control: No written information provided. GPs and pharmacists were requested not to go through the leaflet with the participants or give more spoken information than was usual practice The information was for the drugs (generic names) ß-blocker to lower blood pressure (a chronic condition) , NSAID to treat inflammation of the joints (a chronic condition); or bronchodilator inhaler to treat asthma (a chronic condition). Copy of ß-blocker and bronchodilator inhaler WMIs available. NSAID WMI available in another publication. English language. Evidence based: had been previously piloted.
Outcomes	Knowledge: overall patient knowledge re medicines for 9 questions (aggregated over all study drugs): name medicine; therapy purpose; when to take it; take with fluid; take with food; action if miss dose; store out of reach; safe disposal method; aware not to share medicines Knowledge: overall patient awareness of side effects (aggregated over all study drugs) Attitudinal: overall patient satisfaction response for information received (Aggregated over all study drugs) ; complete satisfaction; satisfaction; indifferent; dissatisfaction; complete dissatisfaction; don't know
Notes	Cluster randomised trial. Total withdrawal: not reported Total loss to follow-up: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Johnson 1986

Methods	Randomisation method: not reported. Baseline comparability: for age, sex, education, previous treatment. Outcome assessor only blinded. One month follow-up.
Participants	USA. 34 adults (mean age 58 years) in a cardiac rehabilitation program taking a study drug (digoxin and/ or propranolol hydrochloride). 80% male, 82% completed high school, 41% completed college
Interventions	Intervention group: one page WMI describing principal organ affected by drug, drug's primary effects, dosing regimen, and common side effects/toxicity. Provider of WMI not reported Control group: No written information provided. The information was for the drugs (generic names) igoxin and/or propranolol hydrochloride, used to treat a variety of chronic conditions. No copy of WMI available. PresumeEnglish language WMI. Not theory or evidence based.
Outcomes	Knowledge: endpoint and change score of knowledge of drug.

Johnson 1986 (*Continued*)

Notes	Two participants in each group were taking both drugs and so were analysed for the outcome measure in each group. This paper conducted two trials. We report only trial 2 as trial 1 did not use allocation. It is not clear from the reporting of the paper if additional spoken information was given or not. It is possible that this was given, but it was not formally linked to the WMI provided Total withdrawal: not reported Total loss to follow-up: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	Inadequate

Knapp 2004

Methods	Randomisation method: adequate. No attempt was made to conceal allocation. Baseline comparability: for age, sex, education, qualification. No blinding. Immediate follow-up.
Participants	UK. 120 adults (mean age 63; range 35 to 74) attending cardiac rehabilitation following cardiac complications and were taking either of the study drugs. 63% male. 56% had no formal education qualification. Excluded if first language was not English or could not read English
Interventions	Intervention 1: written statement about one of two side effects in verbal form as suggested by EU regulation (e.g. this is a rare side effect of the medicine) Intervention 2: written statement about one of two side effects in numerical form (e.g. this side effect occurs in 0.04% i.e. 4 out of 10,000 people who take this medicine) No further spoken information was given. Interventions were stratified by the drug that participants were taking (simvastatin or artovastatin) The information was for the drugs (generic names) simvastatin or atorvastatin, used to lower high cholesterol, a chronic condition. Copy of WMI available. English language WMI. Intervention was not theory based.
Outcomes	Knowledge: estimate of adverse events occurring; estimate of likelihood of occurrence Aittitudinal: perceived risk to health; satisfaction with information; effect on decision to take medicines; severity of side effects
Notes	Patients had been taking the statin for variable periods and may have based responses on their own experience as well as the information provided Total withdrawal: 0/120 (0%) Total loss to follow-up: 0/120 (0%)

Risk of bias

Knapp 2004 (*Continued*)

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	Inadequate

Kumana 1988

Methods	Randomisation method: not reported. Baseline comparability for age, sex, diabetes duration. Outcome assessor only blinded. 3 months follow-up.
Participants	Hong Kong. 111 adults (mean age 56 years) with type 1 or type 2 diabetes attending a diabetic clinic. 37% male
Interventions	Intervention group: 1-page hypoglycaemic WMI: stating need for drug, special instructions for taking medication, what to do if you miss a dose, signs and symptoms of a hypoglycaemic reaction. Interviewed before and after sheet was given. Provider of WMI not reported Control group: No written information provided. The information was for a hypoglycaemic agent, used to treat diabetes, a chronic condition. No generic or trade name was reported. Copy of WMI available. English language on 1 side. Chinese language on 1 side. Not theory or evidence based. 3 months follow-up.
Outcomes	Knowledge: endpoint and difference in patient knowledge on 10 questions
Notes	It is not clear from the reporting of the paper if additional spoken information was given or not. It is possible that this was given, but it was not formally linked to the WMI provided Total withdrawal: not reported Total loss to follow-up: 4/111 (4%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Labor 1995

Methods	Randomisation method: not reported. Baseline comparability: for age, sex, education, previous treatment. Outcome assessor only blinded. One day follow-up.
Participants	USA. 150 adult patrons (mean age 43) from a University medical clinic. 45% had a college degree
Interventions	Intervention 1: PIL: simple wording and 2 topic scope Intervention 2: PIL: simple wording and 12 topic scope Intervention 3: PIL: patient normal wording and 7 topic scope Intervention 4: PIL: professional wording and 2 topic scope Intervention 5: PIL: professional wording and 12 topic scope No further spoken information was given. Information = complexity of wording (simple, patient normal, professional). Scope = amount of information about study drug (2, 7, 12 items). The information was for an antihistamine, (trade name Seldane), used to treat allergic reactions, which is an acute condition. Partial copy of WMI available. English language. Leaflets were evidence-based: revised in a pilot study, and using Flesch reading levels test
Outcomes	Attitudinal: topics judged 'about right'; complexity judged 'about right'; judgemental component; emotional component; evaulative component
Notes	Total withdrawal: 56/150 (37%) Total loss to follow-up: 62/150 (41%) Data are taken from Table 8, p1325.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Little 1998

Methods	Randomisation method: adequate (random numbers table). Baseline comparability: for age, education. Outcome assessor only blinded. Three month follow-up.
Participants	UK. 636 women (mean age 27; range 21 to 31 years) attending a check-up appointment for repeat prescription of combined pill. Excluded if younger than 17 years, unable to complete questionnaire, or if first consultation for contraceptive pill
Interventions	Intervention 1: evidence-based summary leaflet the size of a credit card containing a summary of the rules of the contraceptive pill: aggregated over those receiving and not receiving questions Intervention 2: Family Planning Association leaflet given with no explanation, but endorsed by the

Little 1998 (*Continued*)

	healthcare professional: aggregated over those receiving and not receiving questions Control group: a blank leaflet. The information was for an oral contraceptive pill (a drug group), for chronic use to prevent pregnancy. No generic or trade name was reported. Copy of WMI available. Theory-based. English language
Outcomes	Knowledge: patient knowledge (getting all questions correct)
Notes	Aggregated over those receiving and not receiving questions for each intervention. Missing data and data about the trial conduct was received from author. It is not clear from the reporting of the paper if additional spoken information was given or not. It is possible that this was given, but it was not formally linked to the WMI provided Total withdrawal: not reported Total loss to follow-up: 99/636 (16%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	Adequate

McBean 1982

Methods	Randomisation method: not reported. Baseline comparability: for social demographic characteristics (not specified). Blinded outcome assessment. Three weeks follow-up.
Participants	Canada. Chronically ill adults in receipt of a prescription for a cardiovascular drug, anti-inflammatory drug, or cimetidine
Interventions	Intervention: WMI only dispensed by pharmacist researcher Control: pharmacy control receiving no written information No further spoken information was given. The information was for a cardiovascular drug (a drug group) used in chronic conditions; an anti-inflammatory drug used in chronic conditions; or cimetidine, used to lower acid in the stomach, a chronic condition. WMI copy not available. Presume English language. Not theory or evidence based 3 weeks follow-up.
Outcomes	Knowledge: participant knowledge at follow-up (difference from baseline) Knowledge: median satisfaction with information Behaviour: long-term compliance Behaviour: side effect reported at follow-up (difference from baseline)

McBean 1982 (*Continued*)

Notes	Trial originally had six groups. We only extracted and report data from the two groups which could isolate the effects of WMI. The other four arms did not isolate the effect of WMI. These arms were: written and spoken private information; written and spoken nonprivate information; a second control arm; and written and spoken telephone information Originally 155 participants were randomised to the six interventions, but it is not reported how many were divided into each intervention Total withdrawal: not reported Total loss to follow-up: 41/155 (26%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Morris 1982

Methods	Randomisation method: not reported. Baseline comparability: for age, ethnicity, education, employment. Blinding not reported. Three months follow-up.
Participants	USA. 249 adults (median age 52 years) with newly diagnosed (< 6 months) mild essential hypertension (DBP = 95 to 110 mmHg, no target organ damage). 54% male; 56% black and 33% Spanish-American. Median number of years of schooling = 10.1 years and 39% graduated from high school
Interventions	Intervention: WMI with 6 panels, measuring 9.3 x 21.6cm with orange-shaded illustrations describing the uses and side effects of thiazide drugs, which were grouped according to reason for occurrence. Specific side effects were printed in bold. Provider of WMI not reported Control: No written information provided The information was for thiazide diuretic (a drug group), used to lower high blood pressure, a chronic condition. No generic or trade name was reported. No copy of WMI available. Spanish or English language WMI. Not theory or evidence based.
Outcomes	Knowledge: mean number of side effects correctly named after 2nd follow-up (17* possible side effects) Knowledge: mean number of side effects incorrectly named after 2nd follow-up (17* possible side effects) Knowledge: mean number of health problems reported at 2nd follow-up (17* possible side effects) * Only 10 problems were stated in the WMI
Notes	Intervention aggregated over those receiving and not receiving follow-up interview immediately after or one month after intervention. The paper reports different endpoint denominators for the numbers in each group for the different outcome measures (knowledge and behaviour). It is not clear from the reporting of the paper if additional spoken information was given or not. It is possible that this was given, but it was not formally linked to the WMI provided Total withdrawal: not reported

Morris 1982 (*Continued*)

	Total loss to follow-up: 104/249 (42%)	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Peura 1993

Methods	Randomisation method: not reported. Baseline comparability: for age, sex. Treatment provider only blinded. Followed-up "a few days later".	
Participants	Finland. 500 adults (older than 16 years) in receipt of first time prescription for an antibiotic and purchased themselves. 27% male	
Interventions	Intervention: electronically produced WMI with information in short sentences - dosage instructions, need for finishing course, when to take drug, how to take drug, and mild side effects. Spoken information also given. WMI provided by pharmacist Control: No written information provided. Spoken information given from pharmacists alone The information was for common antibiotics, a drug group; (trade names) Penicillin, Cephalophorins, Erythromicin, Tetra-cycline, and Sulpha-Trimethroprim, prescribed in primary care, and used to treat acute bacterial infections. Copy of WMI available. Presumably Finnish language WMI. Not theory or evidence based.	
Outcomes	Knowledge: participants know what to do if miss a dose Knowledge: participants know tablet taken with water Knowledge: participants know recommendations for drinking alcohol and medication Knowledge: participants know can take sauna during medication Knowledge: participants can name at least 1 correct side effect	
Notes	Total withdrawal: not reported Total loss to follow-up: 87/500 (17%)	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Peveler 1999

Methods	Randomisation method: adequate (block randomisation). Concealment of allocation by opaque sealed envelopes. Baseline comparability: not reported. Outcome assessor only blinded. 12 weeks follow-up.
Participants	United Kingdom. 213 adults (mean age 45 years; range 21 to 83) attending GP for anti-depressant treatment. 27% male. Excluded if in previous receipt of study drug (less than 3 months), if contraindication (concurrent medical condition), or if at risk of committing suicide
Interventions	Intervention: EU directive based WMI about unwanted drug effects, and what to do in the event of a missed dose, distributed by a nurse, aggregated over those receiving or not receiving counselling Control : No written information provided, aggregated over those receiving or not receiving counselling The information was for the drugs (generic names) dothiepin and amitriptyline, drugs used to treat depression, which can be a chronic condition. Copy of WMI available (from author). English language WMI. Not theory or evidence based. 12 weeks follow up.
Outcomes	Behaviour: reported continuation of treatment at 6 months (checked against MEMS device recording when tablet container was opened for dosing event)
Notes	This was originally a factorial design trial. We have aggregated intervention one and intervention two over the other (non-relevant intervention) counselling (provided by a nurse) and no counselling. Attention control arm not included as it would not isolate the effect of WMI Total withdrawal: Not reported Total loss to follow-up: 9/213 (4%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Pope 1998

Methods	Randomisation method: adequate (coin toss). Baseline comparability: mean age, sex, duration taking NSAID, missed dose frequency. Outcome assessor only blinded. 111 days follow-up.
Participants	Canada. 72 adults (mean age 48; range 35 to 62) attending a rheumatology follow-up clinic. 31% male
Interventions	Intervention: written drug information sheet providing information about the function of the drug, side effects, contraindications, and advice on when to call the doctor. Spoken instructions also provided. Provider of WMI not reported Control: No written information provided. Spoken instructions only

Pope 1998 (*Continued*)

	The information was for an NSAID, a drug group used to reduce inflammation, a chronic condition. No generic or trade name was reported. Copy of WMI available. Unclear what language(s) WMI was written in. Not theory or evidence based.
Outcomes	Knowledge: number of side effects listed for NSAIDs Knowledge: number of correct side effects Knowledge: correctly identify: don't take NSAID on empty stomach Knowledge: correctly identify: NSAIDS help with pain Knowledge: correctly identify: don't take ASA with NSAID Knowledge: correctly identify: NSAID decrease inflammation Knowledge: correctly identify: NSAID rarely cause a rash Knowledge: correctly identify: NSAID can cause an ulcer Knowledge: correctly identify: NSAID can cause GI bleed Knowledge: correctly identify: call GP if heartburn occurs Knowledge: correctly identify: call GP if black bowel movement
Notes	Same WMI was given in Savas 2001. A third group received WMI. This was not extracted as it would not isolate the effect of WMI Total withdrawal: not reported Total loss to follow-up: 1/72 (1%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	High risk	Inadequate

Regner 1987

Methods	Randomisation method: not reported. Baseline comparability: not reported. Blinding: not reported. 17 days follow-up.
Participants	USA. 48 adults attending one of three outpatient clinics for a cardiac problem and presenting a new or refill prescription
Interventions	Intervention: spoken and printed information. Printed leaflet endorsed by American Society of Hospital Pharmacists, based on current patient education material. Provider of WMI not reported Control: No written information provided. Spoken instructions given The information was for a drug (generic name) digoxin, used to treat a cardiac condition which is chronic. WMI not available. WMI presumably written in English. Not theory or evidence based.
Outcomes	Knowledge: recognition of side effects caused by the drug

Regner 1987 (*Continued*)

Notes	A 3rd group received WMI alone. This was not extracted as it would not isolate the effect of WMI Total withdrawal: not reported Total loss to follow-up: 14/48 (29%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Robinson 1986

Methods	Randomisation method: not reported. Baseline comparability: not reported. Blinding: not reported. 2 weeks follow-up.
Participants	USA. 100 voluntary participants who were residents in a psychiatric hospital and identified by their treatment teams as ready for discharge to aftercare
Interventions	Intervention: 1 to 2 page presumably English language medication information sheet (not available); specific to the class(es) of medication on which they were being discharged and standard education Control: No written information provided. Spoken information given The information was for drugs (not reported) for treating mental health problems, that is a chronic condition. WMI presumably written in English. Copy of WMI not available. Not theory based.
Outcomes	Knowledge: mean number of five questions answered correctly Behaviour: post-discharge drug compliance
Notes	A further 50 participants were recruited and randomised to receive the WMI which was reviewed with a student nurse or psychology intern. This arm was excluded as it would not isolate the effect of WMI. The differences in the number of participants measured for the knowledge and adherence outcomes was due to them being measured at different points in time, at which point several had dropped out Total withdrawal: not reported Total loss to follow-up: 68/100 (68%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Savas 2001

Methods	Randomisation method: adequate (random number table) Baseline comparability for age and sex. Blinding: not reported. 7 to 10 days follow-up.
Participants	Turkey. 70 adults (mean age 50 years; range 28 to 73) attending outpatient clinic and prescribed NSAID (> 3 per year)
Interventions	Intervention: WMI + spoken information. WMI was presented using the active voice and short sentence (8 to 10 words), and based on standard rules for written patient education material. Information on benefits, side effects (with examples), advice to contact GP, warning not to take 'blood thinning drugs with NSAID, when to stop drugs, rare side effects (with examples), warning not to take on an empty stomach, and to contact rheumatologist for further information. Provider of WMI not reported Control: No written information provided. Spoken information providing the same as information as the leaflet given The information was for a NSAID (a drug group) used to reduce inflammation, a chronic condition. No generic or trade name was reported. Copy of WMI available. WMI presumably written in Turkish. Not theory or evidence based.
Outcomes	Knowledge: number of correct answers in 8-item questionnaire
Notes	Same WMI was given in Pope 1998. A third arm received a PIL only and was not extracted as it was irrelevant to this review because it did not isolate the effect of WMI Total withdrawal: 9/70 (13%) Total loss to follow-up: 9/70 (13%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Strydom 2001a

Methods	Randomisation method: adequate (random number table) Baseline comparability for age, sex, level of IQ and reading ability. Outcome assessor only blinded. 5 weeks follow-up.
Participants	UK. 57 adults (median age 36 years), 63% male, with mild-to-moderate learning difficulties and taking psychiatric medication(s). Excluded people with severe and profound learning disabilities
Interventions	Intervention: WMI + spoken information. WMI contained high quality medication information written simply in large script according to readability guidelines, and illustrated with pictures. WMI provided by a clinician Control: No written information provided. Spoken information given by nurse or psychiatrist.

Strydom 2001a (*Continued*)

	WMI not available; presumably written in English. The information was for one of eight drugs used to treat mental health problems, that is a chronic condition. The generic and trade names for the drugs were not reported
Outcomes	Knowledge: participant knowledge at 5 week follow-up
Notes	Four treatment providers ignored the allocation system and their patients were subsequently withdrawn. Missing data was received from author. Total withdrawal: 5/56 (9%) Total loss to follow-up: 6/56 (11%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

van Haecht 1991

Methods	Randomisation method: adequate (random number table) Baseline comparability: not reported. Outcome assessor only blinded. Length of follow-up unclear: outcome assessors enrolled for 6 months
Participants	Belgium. 366 adults (mean age 38 years; range 14 to 82) with varying levels of school education, attending GP surgery and receiving NSAID treatment for pain. 55% male. 50% 'low', 32% 'middle' and 18% 'higher' level of education. Excluded if less 14 years old, pregnant, or if NSAID contraindicated
Interventions	Intervention one: experimental PIL: explicit headings, lay terminology, simple syntax, with improved readability (type size 9) Intervention two: traditional insert: identical to PIL in every way, bar the specific characteristics above The information was for a drug (generic name) pirprofen, which is an NSAID, used to reduce inflammation, and used here for acute muscle problems. Copy of WMI not available. Dutch language WMI. Not theory based. Length of follow-up unclear, but outcome assessors were enrolled for 6 months. Intervention provided by GP
Outcomes	Behaviour: read the PIL thoroughly:
Notes	We could not include any other outcome measure as they reported only for those who had read the PIL, and not by intervention Total withdrawal: not reported Total loss to follow-up: 49/366 (13%)

Risk of bias

van Haecht 1991 (*Continued*)

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Vander Stichele 1992

Methods	Randomisation method: adequate (block randomisation) Baseline comparability for sex but not age. Blinding not reported. 8 weeks follow-up.
Participants	Belgium. 74 adults (age 52 to 70 years*) with mild-to-moderate essential hypertension (DBP: 90 to 115 mmHg), currently untreated or uncontrolled. 49% male, 100% white. Excluded if recently treated with ß-blocker or ACE inhibitor, or if either treatment was contraindicated, or if suffered recent CVD. * For those not lost to follow-up.
Interventions	Intervention: WMI: information on indication for taking the drug, how to use and dosage, when not to use, unwanted effects, special precautions, pregnancy and nursing a baby, interactions with other drugs, driving and using machines, what to do in the event of an overdose, how to store drug. Treatment provider was GP Control: No written information provided The information was for one of two drugs (trade names), Atenolol or Cisinopril, used to reduce high blood pressure, a chronic condition. (WMI followed same design and information for each drug.) Copy of WMI available. Dutch language WMI. Not theory or evidence based
Outcomes	Behaviour: patient compliance (measured by MEMS device recording when tablet container was opened for dosing event)
Notes	Four treatment providers violated protocol and their six patients were withdrawn. Six of the initial 74 participants were excluded from the trial: 3 were excluded because of flawed data collection, and 3 because of protocol violation. It is not clear from the reporting of the paper if additional spoken information was given or not. It is possible that this was given, but it was not formally linked to the WMI provided Total withdrawal: 18/68 (26%) Total loss to follow-up: 28/68 (32%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Vesco 1990

Methods	Randomisation method: not reported. Baseline comparability: not reported. Blinding: not reported. 8 days follow-up.
Participants	France. 40 adults (mean age 43 years) with treatment naive asthma staying in a nursing home for respiratory patients. 75% male
Interventions	Intervention: package containing manufacturer's instructions. Provider of WMI not reported Control: No information. The information was for a drug (generic name) slow-release theophylline, used to treat asthma, a chronic condition. Partial copy of WMI attached. French language WMI (with English translation for report). Not theory or evidence based
Outcomes	Behaviour: endpoint theophylline blood levels Behaviour: stopped taking medicine (measured by pill count) Behaviour: side effects reported (symptom score per treatment day)
Notes	Total withdrawal: 11/40 (28%) Total loss to follow-up: 3/40 (8%)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Agunawela 1998	Cannot isolate effect of WMI alone
Al-Eidan 2002	Cannot examine effect of written information alone
Al-Rashad 2002	Not an RCT
Al-Saffar 2005	Inadequate randomisation
Anonymous 1999	Trial·examines·a readability formula
Ascione 1984	Does not present data for individual arms
Atherton-Naji 2005	Condition-based information

(*Continued*)

Azrin 1998	Information was for different medicines
Barlow 1997	Condition-based information
Bernardini 2000	Not an RCT
Bernardini 2001	Trial·examines·a readability formula
Berry 1981	Unable to extract meaningful results
Berry 2002	Does not present data for individual arms
Berry 2004	Not patients
Berto 2000	Trial·examines·a readability formula
Bjorck Linne 2001	Cannot examine effect of written information alone
Chin-Quee 2006	Pictogram intervention
Clementsen 1992	Verbal information intervention
Clinite 1976	Not an RCT
Crawford 2003	Not an RCT
Crichton 1987	Not an RCT
Crilly 2005	Condition based information
Culbertson 1988	Not an RCT
Demiralay 2002	Condition-based information
Demiralay 2004	Condition-based information
Discenza 1992	Label study
Eaton 1980	Inadequate randomisation
Edworthy 1999	Trial·examines·a readability formula
Esposito 1995	Cannot examine effect of written information alone
Evans 1996	Not an RCT
Ferguson 1987	Label study

(*Continued*)

Fincham 1995	Medication not widely available
Gardner 1990	Participants were not taking medicines
Halperin 1998	Not an RCT
Hannes 1991	Not an RCT
Hartzema 1999	Unable to extract meaningful results
Harvey 1991	Cannot examine effect of written information alone
Hayes 1996	Information about medicines not of primary focus
Hendler 2003	Verbal information intervention
Hill 2000	Verbal information intervention
Hill 2003	Verbal information intervention
Holcomb 2003	Trial·examines·a readability formula
Hussain 2003	Not an RCT
Hämeen-Anttila 2004	Pictogram intervention
Jacobs 1996	Not an RCT
Jones 2000	Study of illicit drug use
Kelloway 1993	Information about using a medicine appliance
Kirksey 2004	Trial·examines·a readability formula
Kirscht 1981	Condition-based information
Knapp 2005	Pictogram intervention
Krass 2002	Intervention is a method for rating leaflets
Laher 1981	Condition-based information
Lamb 1994	Verbal information intervention
Leal Hernández 2004	Information about a medical appliance
Ley 1976	Not an RCT

(*Continued*)

Lirsac 1991	Information about a medical appliance
Little 2005	Condition-based information
Macfarlane 1997	Decision aids intervention
Macfarlane 2002	Decision aids intervention
Madoff 1996	Computer-based information intervention
Mainous 2000	Participants were not taking medicines
Mansoor 2003	Trial·examines·a readability formula
Mansoor 2006	Inadequate randomisation
Mansoor 2007	Inadequate randomisation
McCormack 2003	Condition-based information
Miquel 2000	Not patients
Morris, 1997	Not an RCT
Morrow 1998	Icon intervention
Mundt 2001	Condition-based information
Murphy 2002	Multicomponent complex intervention
Myers 1984	Cannot isolate effect of WMI alone
Myers 2004	Trial·examines·a readability formula
Neafsey 2002	Not incorporated into usual practice
Ngoh 1992	Icon intervention
Ngoh 1997	Icon intervention
Norrell 1979	Cannot examine effect of written information alone
O'Connell 1995	Trial·examines·a readability formula
Oldman 2004	Medicine is anaesthetic
Pander Maat 1996	Inadequate randomisation

(*Continued*)

Quaid 1990	Evaluation of spoken information by health professional
Rabol 2002	Not an RCT
Rollins 2005	WMI is for different medicines
Ronmark 2005	Information about a medical appliance
Ruck 1990	Participants were not taking medicines
Russell 1979	Communication study
Sands 1984	Not an RCT
Sansgiry 2001	Examines information processing
Satterwhite 1980	Unable to extract meaningful results
Saunders 1991	Written reminders
Savage 2003	Information about a medical appliance
Schaffer 2004	Condition-based information
Segador 2005	Not WMI - reminder to take medicines
Smith 1986	Cannot examine effect of written information alone
Smith 1995	Not an RCT
Smith 1998	Trial·examines·a readability formula
Stratton 1984	Trial·examines·a readability formula
Sukkari 2001	Trial·examines·a readability formula
Suppatiporn 2005	Condition-based information
Swanson 1990	Trial·examines·a readability formula
Sweileh 2004	Unable to extract meaningful results
Temple 1997	Not an RCT
Thomas 1983	Trial·examines·a readability formula
Thomas 1998	Trial·examines·a readability formula

(*Continued*)

Thompson 1988	Not written medicines information
Troller 1989	Not an RCT
Tymchuk 1990	Trial·examines·a readability formula
Udkow 1979	Not an RCT
van Haecht 1990	Not an RCT
Vivian 1980	Trial·examines·a readability formula
Webb 2001	Condition-based information
Webber 2001	Condition-based information
Whatley 2002	Provided hypothetical information
Whiteside 1983	Not written medicines information
Winkler 1981	Unable to extract meaningful results
Wise 1986	Condition-based information
Wiseman 1989	Not an RCT
Worsley 1989	Not an RCT
Young 2006a	Participants were not taking medicines
Young 2006b	Participants were not taking medicines
Zion 1989	Trial·examines·a readability formula
Zondag 2002	Not an RCT
Zweifler 1989	Condition-based information

DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Trial outcome data

Trial	WMI Characteristics	Knowledge outcome	Attitude outcome	Behaviour outcome
Arthur 1998	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Copy of information available	Number who identified drug as NSAID Naprosyn I: 14/38, n = 38 C: 5/36, n = 36 (P < 0.001) Indomethacin I: 10/38, n = 38 C: 5/36, n = 36 (P < 0.001) Ibuprofen I: 22/38, n = 38 C: 14/36, n = 36 (P < 0.01) Naproxen I: 12/38, n = 38 C: 6/36, n = 36 (P < 0.001) Nabumetone I: 11/38, n = 38 C: 8/36, n = 36 (P < 0.01) Ketoprofen I: 5/38, n = 38 C: 5/36, n = 36 (P = NS) Diclofenac I: 16/38, n = 38 C: 9/36, n = 36 (P < 0.001) Relifex I: 10/38, n = 38 C: 10/36, n = 36		

Table 1. Trial outcome data (*Continued*)

		(P < 0.01) Brufen I: 23/38, n = 38 C: 19/36, n = 36 (P < 0.001) Indocid I: 11/38, n = 38 C: 3/36, n = 36 (P < 0.01) Voltarol I: 25/38, n = 38 C: 19/36, n = 36 (P < 0.001) Oruvail I: 7/38, n = 38 C: 7/36, n = 36 (P = NS)		
Baker 1991	* What this medicine is and what it is used for * How to take the drug * Possible side effects * Copy of information available * Theory/evidence based	Recall information before leaving hospital: treatment purpose I: 43/49 (87.8%) C: 21/52 (40.4%) (P < 0.001) action if miss dose I: 30/49 (61.2%) C: 4/52 (7.6%) (P < 0.001) possible side effects I: 34/49 (69.4%) C: 7/52 (13.5%) (P < 0.001) action re side effects I: 26/49 (53.1%) C: 2/52 (3.8%) (P < 0.001) when to take drug I: 46/49 (93.9%) C: 46/52 (88.5%) (P = NS)	Sufficient information felt to have been given: I: 36/49 (73.5%) C: 7/52 (13.5%) (P < 0.001) Information felt to be clear and easy to understand: I: 44/49 (83.7%) C: 17/52 (32.7%) (P < 0.001) Information felt to be useful or extremely useful: I: 41/49 (83.7%) C: 17/52 (32.7%) (P < 0.001) Felt information could be improved: I: 13/49 (26.5%) C: 33/52 (63.5%) (P < 0.001)	

Table 1. Trial outcome data (*Continued*)

		how to take drug I: 38/49 (77.6%) C: 35/52 (67.3%) (P = NS) whether you can drive I: 18/49 (36.7%) C: 14/52 (26.9%) (P = NS) whether you can drink alcohol I: 30/49 (61.2%) C: 16/52 (30.8%) (P = NS)	Reduced worry about drug treatment as a result of specific information: I: 26/49 (53.1%) C: 13/52 (25.0%) (P < 0.05)	
Bergus 2002	* What this medicine is and what it is used for * Possible side effects * Copy of information available * Theory/evidence based		Change in rating of favourability of treatment: I1: -5.2, I2: -10.9 (P = 0.02)	
Clark 1972	* How to take the drug * Partial copy of information available * Theory/evidence based	Understanding of the use of the drug (possible score is 15) I1: 13.9 (SD 1.7) n = 15 I2: 11.1 (SD 3.3) n = 15 C: 10.3 (SD 3.6) n = 15 (P = 0.035 between I1 & C) (P = 0.008 between I1 & I2)		
Desponds 1982	* What this medicine is and what it is used for * How to take the drug * Possible side effects * Copy of information available * Theory/evidence based	Aggregated mean number of questions about the four drugs: % all correct I: 47.0% n = 114 C: 38.5% n = 108 % partly correct I: 27.7% n = 114 C: 24.9% n = 108 % missing I: 12.8% n = 114 C: 16.1% n = 108	Felt text: easy to understand I: 104/114 C: 51/108 (P < 0.01) easy to read I: 106/114 C: 80/108 (P = NS) interesting I: 102/114 C: 84/108 (P = NS) judged to be complete I: 100/114	

Table 1. Trial outcome data (*Continued*)

		% wrong I: 12.5% n = 114 C: 20.5% n = 108	C: 79/108 (P < 0.05) a lot of new information I: 46/114 C: 23/108 (P < 0.05)	
Dodds 1986	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Copy of information available * Theory/evidence based	Median recall of information essential to correct drug taking (max score = 10): I: 7/10, n = 31 C: 4/10, n = 30 (P = 0.0001)		Median patient behaviour questionnaire score for assessing actual drug taking (max score = 17): I: 13/17, n = 31 C: 10/17, n = 30 (P = 0.008) Median patient compliance score (measured by tablet count and interview) (max score = 27): I: 21/27, n = 31 C: 15/27, n = 30 (P = 0.0001)
Dolinsky 1983	* What this medicine is and what it is used for * How to take the drug * Possible side effects * Copy of information available * Theory/evidence based	Correct recognition of drug information. Ampicillin (Max score is 1.00): I1: 0.87 (SD 0.10) n = 19 I2: 0.85 (SD 0.14) n = 18 C: 0.81 (SD 0.11) n = 14 (P = NS) Methyldopa (Max score is 1.00): I1: 0.77 (SD 0.2) n = 28 I2: 0.78 (SD 0.2) n = 29 C: 0.77 (SD 0.15) n = 27 (P = NS)		Correct application of drug information. Ampicillin (Max score is 9) I1: 4.75 (SD 2.02) n = 16 I2: 4.88 (SD 2.18) n = 17 C: 5.11 (SD 2.63) n = 18 (P = NS) Methyldopa (Max score is 13) I1: 8.66 (SD 2.78) n = 32 I2: 8.36 (SD 2.87) n = 28 C: 8.40 (SD 2.66) n = 25 (P = NS)
Gibbs 1989	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Storage * Copy of information available * Theory/evidence based	Overall patient knowledge re medicines for 9 questions (Aggregated over all study drugs) Name medicine: I: 275/419 (65.6%) C: 220/300 (73.3%) (P < 0.05)	Overall patient satisfaction response for information received (Aggregated over all study drugs) Complete satisfaction: I: 294/419 (70.2%) C: 100/300 (33.3%)	

Table 1. Trial outcome data (*Continued*)

		Therapy purpose: I: 408/419 (97.4%) C: 284/300 (94.7%) (P = NS) When to take it: I: 352/419 (84.0%) C: 222/300 (74.0%) (P<0. 001) Take with fluid: I: 321/354 (90.7%) C: 175/200 (87.5%) (P = NS) Take with food: I: 177/232 (76.3%) C: 67/100 (67.0%) (P = NS) Action if miss dose: I: 223/419 (53.2%) C: 104/300 (34.7%) (P < 0. 001) Store out of reach: I: 361/419 (86.2%) C: 234/300 (78.0%) (P < 0. 005) Safe disposal method: I: 341/419 (81.4%) C: 245/300 (81.7%) (P = NS) Aware not to share medicines: I: 380/419 (90.7%) C: 251/300 (83.7%) (P < 0. 005) Overall patient awareness of side effects (Aggregated over all study drugs): I: 160/419 (38.2%) C: 45/300 (15.0%) (P < 0. 001)	Satisfaction: I: 107/419 (25.5%) C: 135/300 (45.0%) Indifferent: I: 9/419 (2.1%) C: 22/ 300 (7.3%) Dissatisfaction: I: 3/419 (0.7%) C: 27/ 300 (9.0%) Complete dissatisfaction: I: 0/419 (0%) C: 5/300 (1.7%) Don't know: I: 6/419 (1.4%) C: 11/ 300 (3.7%) (P < 0.001)	

Table 1. Trial outcome data (*Continued*)

Johnson 1986	* What this medicine is and what it is used for * How to take the drug * Possible side effects * Copy of information available * Theory/evidence based	Endpoint [change score] of knowledge of drug: I: 4.8 (1.3), n = 18 [+1.1 (1.7)*] C: 4.5 (1.3), n = 20 [0 (0.9)] (*P < 0.05)		
Knapp 2004	* Possible side effects * Copy of information available * Theory/evidence based	Pancreatitis Estimate of adverse events occurring: I1: 18.0%, n = 30 I2: 2.1%, n = 30 (95% CI of difference: 8.2 to 23.5) (P < 0.001) Mean ratings (1 to 6 scale) Likelihood of occurrence: I1: 3.3, n = 30 I2: 2.4, n = 30 (95% CI of difference: 0.3 to 1.5) (P < 0.05) Perceived risk to health: I1: 3.4, n = 30 I2: 2.4, n = 30 (95% CI of difference: 0.4 to 1.7) (P < 0.05) Constipation Estimate of adverse events occurring: I1:34.2%, n = 30 I2:8.1%, n = 30 (95% CI of difference: 15.1 to 37.0) (P < 0.001) Mean ratings (1 to 6 scale) Likelihood of occurrence:	Pancreatitis Satisfaction with information: I1: 3.3, n = 30 I2: 4.1, n = 30 (95% CI of difference: 0.08 to 1.6) (P < 0.05) Severity of side effect I1: 3.7, n = 30 I2: 3.3, n = 30 (95% CI of difference: -0.2 to 1.1) (P = NS) Effect on decision to take medicine I1: 3.1, n = 30 I2: 2.5, n = 30 (95% CI of difference: -0.3 to 1.5) (P = NS) Constipation Satisfaction with information: I1: 3.4, n = 30 I2: 4.2, n = 30 (95% CI of difference: -0.3 to 1.6) (P = NS) Severity of side effect: I1: 3.2, n = 30 I2: 2.8, n = 30 (95% CI of difference: -0.5 to 1.3) (P = NS)	

Table 1. Trial outcome data (*Continued*)

		I1:4.2, n = 30 I2:2.6, n = 30 (95% CI of difference: 0.7 to 2.4) (P < 0.001) Perceived risk to health: I1:3.2, n = 30 I2:2.3, n = 30 (95% CI of difference: 0.4 to 1.8) (P < 0.05)	Effect on decision to take medicine: I1: 3.8, n = 30 I2: 2.6, n = 30 (95% CI of difference: 0.7 to 2.2) (P < 0.05)	
Kumana 1988	* What this medicine is and what it is used for * How to take the drug * Copy of information available	Endpoint [change score] in patient knowledge on 10 questions (Max score = 10) I: 5.8 (2.3), n = 56 [+1.3 (1.9)] C: 6.3 (2.0), n = 51 [+1.1 (1.6)] (P = NS)		
Labor 1995	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Copy of information available * Theory/evidence based		Topics' judged "about right": I1: 35% I2: 79% I3: 90% I4: 61% I5: 56% (P < 0.0001) Complexity judged "about right": I1: 35% I2: 63% I3: 98% I4: 44% I5: 44% (P < 0.0001) Summed scores for participi- pants "judgement" (confused, unsure, doubtful, overwhelmed, and foolish) re the information : I1: 10.9, n = 16	

Table 1. Trial outcome data (*Continued*)

			I2: 9.1, n = 19 I3: 12.2, n = 19 I4: 14.6, n = 17 I5: 13.6, n = 17 (P = 0.004) Summed scores for participants "emotional" response (frustrated, angry, anxious, vulnerable, and irritated) re the information: I1: 12.0, n = 15 I2: 9.0, n = 19 I3: 10.9, n = 17 I4: 12.2, n = 17 I5: 12.2, n =17 (P = 0.24) Summed scores for participants "evaluation" (useful, valuable, satisfying, beneficial and helpful) re the information: I1: 16.4, n = 16 I2: 19.2, n = 18 I3: 18.9, n = 20 I4: 16.3, n = 17 I5: 17.5, n = 17 (P = 0.19)	
Little 1998	* How to take the drug * Copy of information available	Patient knowledge (getting all questions correct) : I1: 52/157 (33.1%) I2: 44/186 (23.7%) C: 35/180 (19.4%) I1 & C: (P < 0.05) I1 & I2: (P = NS) I2 & C: (P = NS)		
McBean 1982	No copy of information available. Not theory or evidence based.	Subjects knowledge at follow-up (diff from baseline) I: 49.0% (+4) n = unclear C: 40.0% (+6) n = unclear	Median satisfaction with information (Range 1 to 5) higher score = greater satisfaction: I: 4 C: 3	Side effect reported at follow-up (diff from baseline): I: 28.0% (+9.0) n = not reported. C: 20.0% (-4.0) n = not reported.

Table 1. Trial outcome data (*Continued*)

				Long-term compliance: I: 57.0% n = not reported. C: 55.0% n = not reported.
Morris 1982	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Layout	Mean number of side effects correctly named after 2nd follow-up (17* possible side effects): I: 2.9, n = 102 C: 2.2, n = 69 Mean number of side effects incorrectly named after 2nd follow-up (17* possible side effects): I: 0.15, n = 102 C: 0.12, n = 69		Mean number of health problems reported at 2nd follow-up (17* possible side effects): I: 4.1, n = 102, C: 3.6, n = 53 * Only 10 problems were stated in the WMI
Peura 1993	* What this medicine is and what it is used for * How to take the drug * Possible side effects * Copy of information available	Participants know: What to do if miss a dose I: 194/218 (89%) C: 129/195 (66%) (P < 0.001) Tablet taken with water I: 211/218 (97%) C: 181/195 (93%) (P = NS) Recommendations for drinking alcohol and medication I: 139/218 (64%) C: 51/195 (26%) (P < 0.001) Can take sauna during medication I: 198/218 (91%) C: 170/195 (87%) (P = NS) Name at least 1 correct side effect I: 183/218 (84%) C: 97/195 (50%) (P < 0.001)		

Table 1. Trial outcome data (*Continued*)

Peveler 1999	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Storage * Copy of information available			Patient reported continuation of treatment at 3 months I: 54 (50.9%), n = 106 C: 54 (50.5%), n = 107 (P=NS)
Pope 1998	* What this medicine is and what it is used for * Before taking the drug * Possible side effects * Copy of information available	Number of side effects listed for NSAIDs: I: 0.6 (0.8), n = 34 C: 1.2 (1.1), n = 37 (P = 0.02) Number of correct side effects: I: 0.5 (0.6), n = 34 C: 0.8 (0.8), n = 37 (P = 0.09) Correctly identify: Don't take NSAID on empty stomach I: 29/30 (96.7%) C: 35/35 (100%) (P = 0.06) NSAIDS help with pain: I: 29/33 (87.9%) C: 23/34 (67.6%) (P = 0.05) Don't take ASA with NSAID: I: 16/31 (51.6%) C: 20/36 (55.6%) (P = 0.9) NSAID decrease inflammation: I: 28/33 (84.9%) C: 33/36 (91.7%) (P = 0.3) NSAID rarely cause a rash: I: 13/33 (39.4%) C: 14/		

Table 1. Trial outcome data (*Continued*)

		36 (38.9%) (P = 0.9) NSAID can cause an ulcer: I: 29/34 (85.3%) C: 24/33 (72.7%) (P = 0.1) NSAID can cause GI bleed: I: 16/33 (48.5%) C: 14/36 (38.9%) (P = 0.5) Call GP if heartburn occurs: I: 16/32 (50.0%) C: 21/37 (56.8%) (P = 0.5) Call GP if black bowel movement: I: 27/34 (79.4%) C: 29/37 (78.4%) (P = 0.9)		
Regner 1987	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Storage	Recognition of side effects caused by the medication: I: 1.8 (1.2), n = 15 C: 0.8 (0.8), n = 19 (P < 0.05)		
Robinson 1986	No copy of the information available.	Mean number of five questions answered correctly I: 4.38 (n = 50) C: 3.20 (n = 50) ANOVA with post-hoc Scheffe test shows I and C are significantly different (P < 0.05)		Post-discharge medication compliance I: 4.32 (n = 16) C: 3.88 (n = 16) ANOVA with post-hoc Scheffe test shows I and C are significantly different (P < 0.05)
Savas 2001	* What this medicine is and what it is used for * Before taking the drug * Possible side effects * Theory/evidence based	Number of correct answers in 8q questionnaire: I: 6.8 (0.9), n = 31 C: 5.2 (1.5), n = 30		

Table 1. Trial outcome data (*Continued*)

		(P = 0.0001)		
Strydom 2001a	* Theory/evidence based	Patient knowledge at 5 weeks: I: 6.8 (2.1), n = 24 C: 6.9 (2.3), n = 26 95% CI for difference of means: (-1.4 to 1.2) (P = 0.89)		
van Haecht 1991	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Storage			Read the PIL thoroughly: I1: 51/161 (31.7%) I2: 38/156 (24.3%) (P = 0.15)
Vander Stichele 1992	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Storage * Layout * Copy of information available			Patient compliance (measured by MEMS device recording when tablet container was opened for dosing event): I: 19/22 (86.4%) C: 17/24 (70.8%) (P = NS)
Vesco 1990	* What this medicine is and what it is used for * Before taking the drug * How to take the drug * Possible side effects * Storage * Copy of information available			Endpoint theophylline blood levels: I: 7.6 µgml-1 (3.13), n = 18 C: 7.8 µgml-1 (3.58), n = 19 (P = NS) Stopped taking medicine (measured by pill count): I: 8/18 C: 3/19 (P = NS) Side effects reported (symptom score per treatment day): I: 0.7 (0.58), n = 18 C: 0.3 (0.31), n = 19 (P < 0.05)

I: Intervention group

C: Control group

APPENDICES

Appendix 1. MEDLINE (Ovid) search strategy

1. Drug Therapy/
2. exp Pharmaceutical Preparations/
3. exp Pharmaceutical Services/
4. exp Pharmacists/
5. exp Prescriptions, Drug/
6. exp Drugs, Non-Prescription/
7. exp Self medication/
8. prescription$1.ti,ab.
9. nonprescription$1.ti,ab.
10. over the counter.ti,ab.
11. (OTC not (organotin or ortnithine or oxytetracycline)).tw.
12. ((drug$1 or medication$) adj3 (information or instruction$ or education$ or advice or advise$)).tw.
13. or/1-12
14. Drug Labeling/
15. exp Drug Packaging/
16. Pamphlets/
17. Teaching materials/
18. Product Labeling/
19. (drug$1 adj2 label?ing).tw.
20. pamphlet$1.ti,ab.
21. (medicines adj2 (information or instruction$ or advice or advise$ or educat$)).tw.
22. leaflet$1.ti,ab.
23. (patient$1 adj2 (information or instruction$ or advice or advise$ or educat$)).tw.
24. (consumer$1 adj2 (information or instruction$ or advice or advise$ or educat$)).tw.
25. (written adj2 (information or instruction$ or advice or advise$ or educat$)).tw.
26. (print$ adj2 (information or instruction$ or advice or advise$ or educat$)).tw.
27. booklet$1.ti,ab.
28. brochure$1.ab,ti.
29. Patient education/
30. (pack$ adj3 insert$1).tw.
31. (prescri$ adj2 information leaflet$1).tw.
32. or/14-31
33. 32 and 13

Appendix 2. Data combination methodology

Analysis of outcomes will be based on intention-to-treat results where possible. A weighted mean treatment effect will be calculated across trials using Cochrane RevMan software. The results will be expressed as Peto odds ratios and 95% confidence intervals (CIs) for dichotomous outcomes, and weighted mean differences and 95% CIs for continuous outcomes. Sensitivity analysis will be performed on the basis of methodological quality and to test for heterogeneity in the results.

WHAT'S NEW

Last assessed as up-to-date: 28 March 2007.

Date	Event	Description
14 September 2011	Amended	Contact details updated.

HISTORY

Protocol first published: Issue 2, 2000

Review first published: Issue 2, 2009

Date	Event	Description
28 April 2009	Amended	Minor editing.
3 November 2008	Amended	Converted to new review format.
12 May 2005	New citation required and major changes	The protocol for this review was first published on issue 2 2000 of *The Cochrane Library* by Knapp P, Raynor DK, Forster A, Henley J. The protocol was updated extensively on issue 3 2005 by Knapp P, Raynor DK, Nicolson DJ, Blenkinsopp A, Grime J, Pollock K, Spoor P, Gilbody S, Maule J, Dorer G, Dickinson D

CONTRIBUTIONS OF AUTHORS

PK, DKR & DJN conceived the idea for the review.

DJN and PK wrote all drafts.

PK will act as guarantor.

DJN and PK abstracted all data.

DJN and PK analysed the results.

PS devised the search strategy.

All authors read and commented on all drafts of the review.

DECLARATIONS OF INTEREST

PK and DKR are directors of Luto Research Ltd, which provides patient information leaflet testing services to the pharmaceutical industry. PK and DKR are authors of a trial included in this review (Knapp 2004); data for this trial were extracted by DJN and a 3rd party (AB).

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Health Technology Assessment, UK.

This funding paid for DJN's salary as a research assistant on the HTA report, from which this review has arisen. It also contributed to the salaries of a second research assistant and a research secretary on the same project.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- In the protocol we stated that the review would include randomised controlled trials (RCTs) in the first instance, with non-randomised controlled trials, controlled before and after studies and interrupted time series studies to be considered in the absence of RCTs. As a number of RCTs were identified for inclusion, we did not extend the selection criterion beyond RCTs, since these provide a more robust level of evidence (see Types of studies).

- For the 'Types of Interventions' selection criterion, we slightly revised the approach we had outlined in the protocol for this review, and instead interpreted 'medicines information' as information fulfilling at least one of the five European Union requirements of mandatory leaflets supplied with medicines (EC 2004) (see Types of interventions).

- We added as a secondary outcome, changes in patients' attitudes towards taking the medicine (see Types of outcome measures).

INDEX TERMS

Medical Subject Headings (MeSH)

*Drug Labeling; *Health Knowledge, Attitudes, Practice; *Nonprescription Drugs [adverse effects; therapeutic use]; *Prescription Drugs [adverse effects; therapeutic use]; Patient Education as Topic [methods]; Randomized Controlled Trials as Topic

MeSH check words

Humans