
Drug Utilization Studies
Focus on Questionnaire Design

**Dissertation presented in Faculdade de Medicina da
Universidade do Porto, to obtain graduation in Master in
Epidemiology**

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This dissertation is based in two manuscripts. In the first manuscript I actively collaborated in the conception, design, acquisition, analysis and interpretation of data, and in the second manuscript I actively collaborated in the analysis and interpretation of data. I was responsible for the first versions of both manuscripts.

- Questionnaire design and the recall of pharmacological treatments: a Systematic Review.
- Effect of two different structures of questionnaire on recall of drug utilization in a population of University Students.

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Background

Drug utilization was defined by the World Health Organization (WHO) as the «marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences»¹. Studies on the process of drug utilization focus on the factors related to the prescribing, dispensing, administering, and taking of medication, and its associated events, covering the medical and non-medical determinants of drug utilization, the effects of drug utilization, as well as studies of how drug utilization relates to the effects of drug use, beneficial or adverse²⁻⁴. The therapeutic practice is expected to be primarily based on evidence provided by pre marketing clinical trials, but complementary data from post marketing period are needed to provide an adequate basis for improving drug therapy⁵.

The interest in drug utilization studies began on both sides of the Atlantic in the early 1960s³, and is still increasing^{6,7}. The first investigations^{5,8,9} were conducted mostly for marketing purposes and data were not widely available for use by academic researchers or health authorities. The boost in the marketing of new drugs, the wide variations in the pattern of drug prescribing and consumption, the growing concern about the delayed adverse effects, and the increasing concerns regarding the cost of drugs, as reflected in the increase of both the sales and the volume of prescriptions all contributed to the increasing importance of drug utilization studies¹⁰⁻¹³.

In the United States drug utilization research has been primarily developed at an institutional level or as part as local health programs³. Initially a great emphasis was placed on the study of the quality of physician prescribing habits, in particular with respect to antibiotics, in both hospital and outpatient settings^{8,9,14}. In Europe, the Scandinavian countries, Scotland, and Northern Ireland^{9,15,16} pioneered the research at the national and international levels. The European drug utilization studies have been predominantly quantitative, describing and comparing patterns of use of specific groups of drugs according to geographic regions and time, showing wide variations in the

utilization of drugs pertaining to several pharmaceutical classes (*e.g.*: anti-diabetics ¹⁵, psychotropics, nonsteroidal anti-inflammatory drugs [NSAIDS] ¹⁷, antihypertensive drugs, antibiotic drugs ¹², and lipid-lowering drugs ¹⁸).

Scope of Drug Utilization Studies

Drug utilization studies may include descriptive epidemiological approaches to the study of drug utilization, but also the assessment of how drug utilization relates to the effects of drug use, beneficial or adverse.

The research in this field aims to analyse the present state and the developmental trends, of drug usage at various levels of the health care system, whether national, regional, local or institutional. Drug utilization studies may evaluate drug use at a population level, according to age, sex, social class, morbidity, among other characteristics. These studies are useful to provide denominators to calculate rates of reported adverse drug reactions, to monitor the utilization of drugs from therapeutic categories where particular problems can be anticipated (*e.g.*, narcotic analgesics, hypnotics and sedatives, and other psychotropic drugs), to monitor the effects of informational and regulatory activities (*e.g.*, adverse events alerts, monitoring urgent safety restrictions). Drug utilization data may be used to produce crude estimates of disease prevalence (*e.g.*, cardiovascular disease ¹⁹, antidiabetic drugs ²⁰), to plan drug importation, production, and distribution, and to estimate drug expenditures.

The characterization of drug utilization may be extended linking prescription data to the reasons for the drug prescribing. They include the concept of appropriateness ^{3,8,9,14} that must be assessed relative to indication for treatment, concomitant diseases (that might contraindicate or interfere with chosen therapy) and the use of other drugs (interactions). Therefore they can document the extent of inappropriate prescribing of drugs (*e.g.* antibiotics, NSAIDs) and even the associated

adverse clinical, ecological, and economic consequences^{8,9,21,22}. Moreover, they can also explore the percentage of drugs that adhere to the evidence-based recommendations in place for its indications^{23,24}.

Data sources

A considerable amount of data on drug usage is available as part of databases with administrative, commercial or clinical purposes, and specific investigations may be conducted to collect different types of information, qualitatively and quantitatively, or referring to a particular population.

The **databases** currently available for purposes of drug utilization studies may be classified as non-diagnosis-linked or diagnosis-linked³. While the latter consider drug utilization linked to its indications and outcomes (e.g. treatment of peptic ulcer²⁵, trends in prescribing for heart failure²⁶), the former concerns only about describing drug consumption in a population (e.g. use of antimicrobial drugs²², statin consumption¹⁸).

Most of currently available data sources lack information on morbidity and are mostly used for generating drug statistics and descriptive studies of patterns of drug consumption. Some collect data in the form of drug sales (e.g., The Portuguese National Authority for Medicines and Health Products (INFARMED), the Danish Medicines Agency, the National Agency for Medicines and Social Insurance in Finland, the Norwegian Institute of Public Health, the National Corporation of Pharmacies in Sweden,), drug movement at various levels of the drug distribution channel (e.g., IMS-Health [www.imshealth.com]), pharmaceutical or medical billing data or all prescriptions dispensed (Prescription Pricing Authority in the UK, Spain's Drug Data Bank, Medicaid Management Information System). However, since most statistics on drug consumption were compiled for administrative or commercial reasons, the data are usually

expressed in terms of cost or volume of sales in units or weight that, although useful for measuring or comparing the economic impact of drug use, does not provide information on the amount of drug exposure in the population. Tablet sizes vary, making it difficult to translate weight into even the number of tablets. Prescription sizes also vary, so it is difficult to translate number of tablets into the number of exposed patients³. The WHO Drug Collaborating Centre for Drug Statistics, intend the use of the defined daily dose (DDD) as a technical unit of consumption to be employed in these type of studies²⁷.

The information on sales available through **pharmacy records** is the measure most frequently used in drug utilization studies^{16,18,20}. They provide detailed information on the drugs themselves although data on the consumer is usually very limited. This could be improved if a patient is allowed to purchase drugs at only one designated pharmacy, as is the case of the Netherlands, where reimbursement regulations require accurate recording of pharmacy data²⁸. But even in this situation, information such as the indication for use or extent to which patients actually consume the drugs will remain largely unknown and it should be noted that all these units represent approximate estimates of true consumption³. The County of Jämtland Project (Sweden) is an example of longitudinal patient-specific studies of drug utilization^{16,29,30}. All drug prescriptions dispensed to 14% of the Jämtland population (approximately 17 000) have been continuously monitored since 1970. The recorded information includes the patient's unique identity number; name, dosage, quantity, and price of the drug; date of dispensing; dispensing pharmacy; and prescribing physician. Information relating to morbidity (diagnoses), however, is missing.

The Odense Pharmacoepidemiologic Database (OPED) and the pharmacoepidemiology prescription database of the County of North Jutland are two similar databases that include about half a million inhabitants in Denmark³¹. These databases contain all dispensed prescriptions since the early 1990s. The following

information is captured for each prescription: a unique person identifier, the date of dispensing, identification of the dispensed product, the pharmacy, and the prescriber. The databases do not include information on over-the-counter medications (laxatives, analgesics, ibuprofen, antihistamines, antitussives, and certain antacids) and non-subsidized drugs (oral contraceptives, hypnotics, and sedatives). They have been used for a number of population-based pharmacoepidemiologic surveys such as the use of the new antidepressants¹³, inappropriate use of inhaled steroids in asthma treatment³², inappropriate use of sumatriptan³³ and low use of long-term hormone replacement therapy³⁴.

The Community of Tierp Project is run by the Center for Primary Care Research, University of Uppsala, Sweden. Prescription and morbidity data are routinely collected from all pharmacies and the health center within the community for all residents since 1972. The Swedish prescribed Drug register is a new register that contains data on all dispensed prescriptions for the entire Swedish population (about 9 million inhabitants) linking to the use of a unique personal identification number⁷. The register does not include data on over-the-counter drugs, herbal drugs, drugs used in hospitals or from drugs storerooms sometimes used in nursing homes. It has information about individual's age, sex and dispensed drugs (amount of drug, date of redemption and dosage, *i.e.* from the prescription written by the prescriber).

The Portuguese National Pharmacy Association (ANF) has also been developing an interesting work. It has created since 1994 a centre for pharmacoepidemiology studies (CEFAR) and a database containing information on medicine consumption, based on dispensing data information from the Portuguese pharmacies. It has been conducting several drug utilization studies with a number of published work addressing different drug utilization issues such as self-medication^{35,36} and antiasthmatics usage³⁷.

Data from **general practitioners (GP)** records of prescriptions can be more informative about the indication for drugs prescribed, diagnoses and other health-related data, although these records are not always consistently completed ²⁸. The National Disease of Therapeutic Index (NDTI), by IMS America, is an ongoing study of physician prescribing which is conducted mainly for use by pharmaceutical companies in their marketing activities ³⁸. This study employs a rotating sample of office-based physicians who record all patient encounters and corresponding «drug mentions» for two-day periods, four times a year. A special prescription form is used to collect information on the drug (specific product, dosage form, new versus continuing therapy), patient characteristics (sex), prescriber (speciality, location, region), type of consultation (first versus subsequent), concomitant drugs and diagnoses, and the desired pharmacological action. Data has been made available to Academic Researchers and the US Food and Drug Administration ¹¹. Although useful for studies of prescribing, longitudinal patient-specific studies are not possible with this database.

The Integrated Primary Care Information (IPIC) database, established at Erasmus University in The Netherlands, consists on the computer-based patient records of 150 general practitioners. To date the database has accumulated data on approximately 500 000 patients. This database has been used to study preventive strategies in patients receiving NSAIDs ³⁹ and trends in primary care prescribing for heart failure ²⁶.

The Tayside Medicines Monitoring Unit (MEMO) and the General Practice Research Database (GPRD), in the United Kingdom, are databases developed primarily for drug safety studies, but have also been used to study drug utilization ⁴⁰. GPRD exists since 1987, and is still growing in the number of practitioners contributing data from over 460 general practitioners, covering about 5.5% of the population of UK (3.5 million currently active research quality patients) being today the most published database ⁴¹.

In Portugal, the National Observatory of Health (ONSA) analyses data related to health status and its determinants among the Portuguese residing population⁴². It has a primary care surveillance network including 150 General Practitioners across the country and has some published drug utilization studies regarding use of several therapeutic classes such as antibacterials⁴³, antiepileptics and antidepressives^{44,45} and antacids²⁵. It has also an observational instrument created with the purpose of obtaining data and indicators on health with the help of a sample of Portuguese families with land-line telephones (“ECOS”).

Data on drug utilization may be obtained directly from the population through **Health surveys**, including national surveys such as Statistics Canada’s National Population Health Survey, or the Portuguese National Health Survey (also from the National Observatory of Health), or smaller surveys conducted in specific settings such as among university students⁴⁶, female population⁴⁷ or elderly outpatients⁴⁸. Such studies provide information on drug use from consumers themselves⁴⁹, and are a source of data on many other health-related issues²⁸.

Instruments for data collection on drug utilization

Patient files and computer registries are widely used as instruments for collecting information on drug utilization. Home inventories are also used and considered by some authors as the best method of obtaining accurate and complete drug use data^{19,50,51}. In this scenario, an interviewer visits the home of the respondent and lists all the drugs in the medicine cabinet. Questionnaires, however, are one of the easiest tools for data collection on drug utilization and the most widely used in population surveys.

Self-reported data in epidemiological studies obtained through **questionnaires** is commonly used as a source of drug exposure information⁵². Data collected by self-

report is, however, subject to recall inaccuracy^{50,53-55}. In some questionnaire-based studies only a limited number of drug categories were evaluated⁵³⁻⁵⁵. In others, the completeness and quality of reference sources were debatable^{56,57}. In several studies questionnaire information was compared with pharmacy records^{53,54}, which are a reliable source of drug exposure, with an acceptable degree of agreement^{28,51,52,58,59}. Despite being accurate, carefully constructed questionnaires can be subject to recall bias due to its characteristics, and noncompliance can also influence the reliability. Furthermore, questionnaire design also influences recall and may lead to different estimates on drug exposure^{50,52,53,55}.

Aims

Drug utilization data collected through questionnaires is commonly used in epidemiological studies but variations in questionnaire structure may affect recall. Therefore, in addition to a careful design of the data collection instruments, the characteristics of the questionnaires used to obtain information on medicines need to be taken into account in the interpretation of results from studies quantifying drug utilization by self-report.

This dissertation addresses the relation between questionnaire characteristics and the recall of pharmacological treatments by participants in drug utilization studies.

The specific objectives of the two manuscripts that compose this dissertation were:

- 1) To review systematically the published evidence on the effect of questionnaire design on the recall of pharmacological treatments;
- 2) To compare the recall of medication use evaluated with two questionnaires differing in structure and length (long questionnaire including indication/drug specific questions vs. short questionnaire including one open ended question and several examples of indications and drugs).

**Questionnaire design and the recall of pharmacological
treatments: a systematic review**

Abstract

Background

Modes of data collection by questionnaire may influence the quality of information, and the utilization of medicines has specific features (*e.g.*, complexity of treatment regimens, disease severity) requiring a careful design of the questionnaires to ensure unbiased evaluations.

Objectives

To review systematically the published evidence on the effect of questionnaire design on the recall of pharmacological treatments.

Methods

The electronic databases Pubmed®, EMBASE™ and Cochrane® Library were searched from inception to October 2007, using the following search terms: *drug utilization, pharmaceutical preparations, pharmacoepidemiology, validation studies, methods, epidemiologic methods, interviews, data collection and questionnaires*. Drug utilization studies comparing different types of questionnaire or methods/strategies of questionnaire administration were included in the review. Backward and forward citation tracking were also conducted to identify potential eligible articles.

Results

Eight studies were included in the systematic review. Six evaluated the effect of asking for specific drugs or indications in the ascertainment of drug exposure, and two either addressed the effects of question order or response choice order. With the exception of two studies conducted in the post-pregnancy setting, the remaining evaluated adult populations. In four studies information was collected by personal or telephone interview, and a self-administered questionnaire was used in the remaining. The recall period varied from current use to medication used in a preceding disease episode. In five of the studies all classes of drugs were evaluated, two of them including over-the-

counter drugs or herbal products, and three questionnaires addressed specific drug groups (analgesics or antimalarials).

Overall, recall was increased in 6,3 to 47% when specific drug names or indications were asked rather than an open-ended question, and in 8,55% when drug was presented first instead of last in a list of choices. Mean enhanced recall also increased in 14, 4% for drug name rather drug category.

Conclusions

Scientific work regarding methods for drug utilization data collection is scarce, particularly when addressing methods for elaborating drug utilization questionnaires in the general population. The existing evidence supports that it is important to avoid using open-ended questions, and rely more in drug names and indications or even pictures as memory aids than on drug categories.

Background

Drug utilization is defined by the World Health Organization (WHO) as the «marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences»¹. Despite the ample scope for research in this field, drug utilization studies all require the measurement of drug use in specific populations. The option for a particular approach, from pre-existing non-diagnosis-linked or diagnosis-linked databases³ to health surveys conducted for this specific purpose, depends on the objectives of the study and the availability of the necessary resources.

Databases on the sales of medicines are usually comprehensive in its coverage of different drug groups and wide geographical regions, and allow trend evaluations and economic assessment of the process of drug utilization. However, these provide information ecological in its nature not allowing inference at individual level³.

Pharmacy records are frequently used as source of data to drug utilization studies^{16,18,20}, but databases linking the information on the use of medicines with the patients' characteristics are often unavailable, and may not always distinguish between patients receiving a different number of prescriptions in any given time interval, or between irregular and chronically used medication (translated as first and refill prescriptions). Data regarding the acquisition of medicines in the pharmacy underestimates true consumption, as the latter ultimately depends on the patients' adherence to treatments³. Data from general practitioners' records are more informative about indication of drugs prescribed and diagnosis^{26,41,44}, but are often incomplete²⁸ and information is not necessarily collected following standard procedures. The information on prescriptions also underestimates true consumption, more strongly than pharmacy records, as the prescriptions do not always correspond to acquired medicines³.

Health surveys⁴⁹ provide information on drug use from consumers themselves. Home inventories are considered a good method to obtain accurate and complete drug use data^{3,19,50,51} but questionnaires are more frequently used as a source of drug exposure information^{50,52,53,55}. Modes of data collection by questionnaire differ in the medium of delivering the questionnaire to respondents and in the administration of the questions, both influencing the quality of information⁶⁰. The utilization of medicines has specific features related to the acute or chronic nature of the diseases and their severity, the number of drugs available for the same condition, the number of medicines including the same drugs, and the varying complexity of the treatment regimens, all requiring a careful design of the questionnaires to ensure unbiased evaluations. Therefore, we aimed to review systematically the published evidence on the effect of questionnaire design on the recall of pharmacological treatments.

Methods

The electronic databases Pubmed® (<http://www.ncbi.nlm.nih.gov>), EMBASE™ ([endereço eletrônico](#)) and Cochrane® Library ([endereço eletrônico](#)) were searched from inception to the 19th October 2007 using the following expression: ((drug utilization OR pharmaceutical preparations OR pharmacoepidemiology) AND (validation studies OR methods OR epidemiologic methods OR interviews OR data collection OR questionnaires) AND humans). Except for “drug utilization” and “pharmacoepidemiology”, all the other search terms were processed in Pubmed as MeSH terms. One reviewer (HG) screened the reference lists following previously established exclusion criteria. To be eligible for the systematic review, the studies had to meet all the following criteria: (i) comparison of different types of questionnaire or methods/strategies of questionnaire administration (ii) evaluation of questionnaires quantifying drug utilization.

Studies written in English, Portuguese, Spanish, French, German or Italian were included in the review, and information was collected from the English abstracts of articles written in other languages.

The reference lists of the articles eligible for systematic review after Pubmed[®], EMBASE[™] and Cochrane[®] Library search were also reviewed, and forward citation tracking, both in ISI Web of Science[®] (<http://apps.isiknowledge.com>) and Scopus[™] (<http://www.scopus.com>) were used to search for articles citing those selected for the systematic review with the remaining search strategies. The same selection criteria were used for references identified by the initial database search and by forward and backward citation tracking.

One author screened the reference lists (HG) and the two authors independently extracted data on the objective and design of the studies, participants, drugs studied, main results and conclusions, with disagreements resolved by consensus.

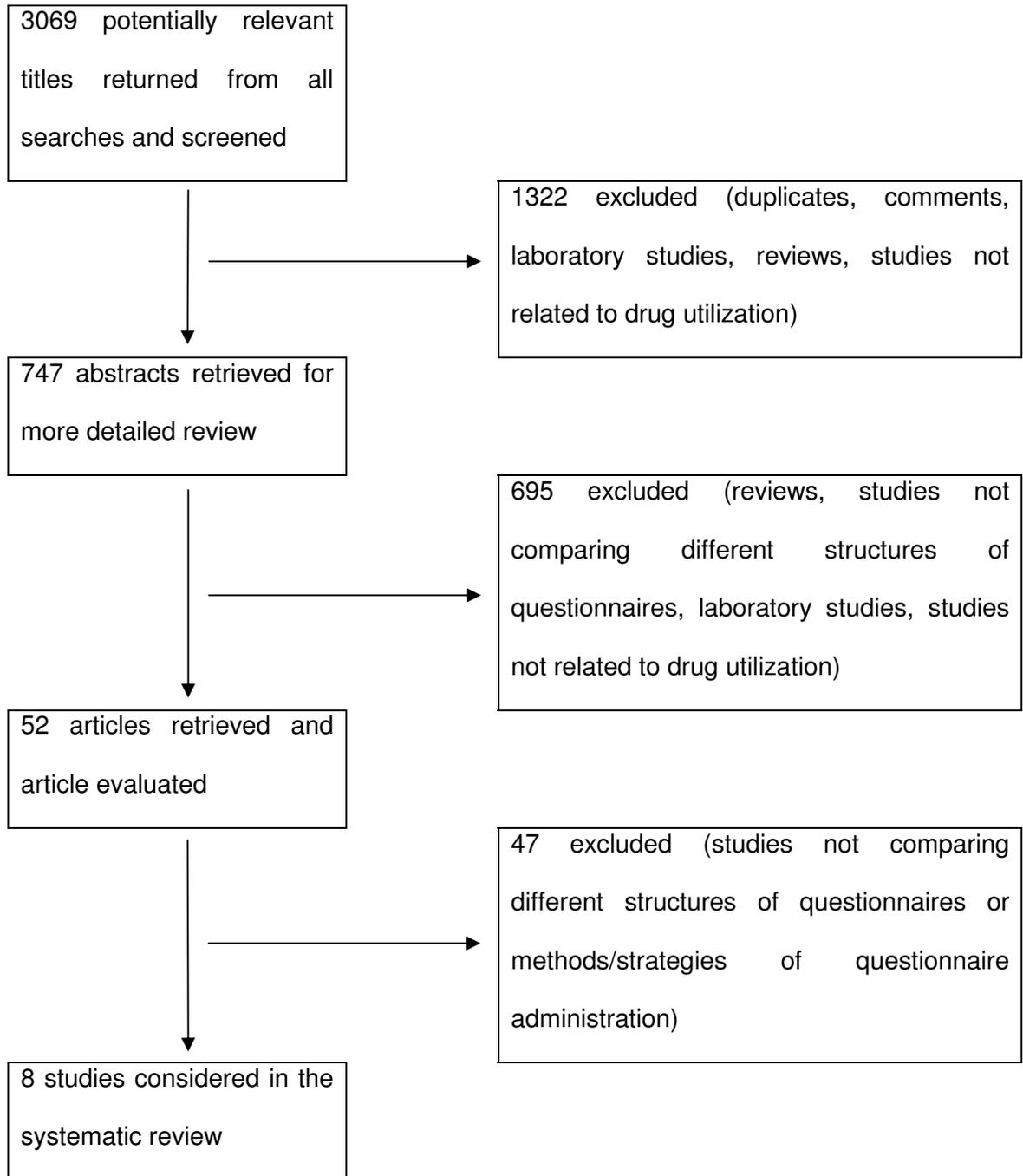
Results

The searches returned 3069 potentially relevant articles. After review of the titles and removal of duplicates, 747 abstracts were read. 52 articles were selected for further evaluation and eight were included in the systematic review. The systematic review flowchart is displayed in Figure 1.

The eight studies evaluated for this review are summarized in table 1. Two were conducted in the USA^{61,62}, two in the Netherlands^{52,63} and the remaining four in different countries: Switzerland⁶⁴, Canada²⁸, Mozambique⁶⁵, and Finland⁶⁶.

Five studies^{28,52,62,63,66,67} evaluated the effect of asking for specific drugs or indications in the ascertainment of drug exposure. One study each addressed the effects of question order⁶⁴ or response choice order⁶⁵, and another evaluated the effect of memory aids on recall⁶¹.

Figure 1. Systematic review flowchart



Two studies were conducted after pregnancy^{62,63} and the remaining evaluated adult populations, one of which studying only hypertensive subjects⁵² and another including only non-aspirin NSAIDS⁵². In four studies information was collected by personal^{62,63} or telephone^{28,61} interviews, and four investigations used self-administered questionnaires^{52,64-66}.

The recall period varied between the studies, from currently used medication⁵², medication used in the previous week^{61,64,66}, in the previous month²⁸ or in a gestation period^{62,63}, to drugs used in a previous condition⁶⁵.

In five of the studies^{28,52,62-64,67} different classes of drugs were evaluated, two of them including over-the-counter drugs or herbal products^{63,64}. Three questionnaires were directed to specific drug groups, namely analgesics^{61,66} and antimalarials⁶⁵.

The reviewed studies addressed the effects different questionnaire structures or mode of administration on the recall of drug use, comparing questionnaires asking for specific drugs or indications with open-ended questions, evaluating the use of memory aids, or studying the influence of question and response order on recall.

Asking for specific drugs or indications

*Van den Berg et al.*⁶³ and *Mitchell et al.*⁶² compared questions in an interview on drug use in pregnancy and found that questions involving indication for use and drug-specific questions were associated with a higher prevalence of drug use when compared to open-ended questions. So did *Neutel et al.*²⁸, *Klungel*⁵² and *Ademi et al.*⁶⁶, who concluded that the prevalence of drug usage was higher when the specific name of the drug rather than the drug category was asked. For *Klungel et al.*⁵² the sensitivity of recall of drugs in the questionnaire was much better for directed recall than for the open-ended question (88% vs. 41%) when comparing open-ended questions to drug-specific questions. *Neutel et al.*²⁸ had a mean increase in accuracy of 14.4%, while *Ademi et al.*⁶⁶ concluded that the best results obtained by asking the name of the medicines.

Only *Klungel*⁵² and *Van den Berg*⁶³ used another source of data collection for comparison, the pharmacy data, and observed a good reliability between the two methods.

Use of memory aids

*Kimmel et al.*⁶¹ associated the reading of medication lists with medication pictures and enhanced recall in 6.3% with memory aids in comparison to a simple question.

Question and response choice order effects

The order of presentation of questions for different types of medication was assessed by *Gmel et al*⁶⁴ with two questionnaire versions regarding the use of drugs or herbal products in the previous 7 days with a list of medicines followed by herbal products and vitamins in one version and herbal products and vitamins presented first in the other version. A preceding question regarding the use of drugs in the previous seven days (skip question) was introduced in the two versions: Version A presented first the skip question followed by all medications and in Version B the skip question separated herbal products and vitamins from the list of medicines. The participants recalled the use of vitamins about twice more frequently with version B of the questionnaire.

*Lunet et al*⁶⁵, prepared two different versions of the same questionnaire regarding use of antimalarial treatment to test response choice order effects. In one version quinine and most frequently used drugs were presented first; while in the other less frequently used drugs were first and quinine were presented at the end. Both authors concluded that when the most frequently used drugs were placed at the end of a list of choices, there was an increase in reported prevalence of drug usage.

Discussion

Questions involving indication for use and drug-specific questions increased the prevalence estimates for drug use in 6.3 to 47% compared to an open-ended question.

Mean enhanced recall was also increased by 14.4% for drug name compared to drug category. Regarding question and response choice order, the medicines listed first were more likely to be selected.

We identified eight published articles comparing different questionnaire designs or methods/strategies of questionnaire administration when addressing the utilization of pharmacological treatments. Nevertheless, our search strategy included three of the electronic databases more likely to include articles on this topic and was designed to be highly unspecific, as shown by the fact that 341 references had to be screened to identify each of the studies included in the review. Also, backward and forward citation tracking of the eligible articles was used to increase sensitivity. The small number of studies available regarding the influence of questionnaire design and its administration in the process of answering questions is also seen in other social, health and epidemiological research based in survey questionnaires⁶⁰, and therefore is not surprising.

The retrieved papers all mention that the completeness of recall and the degree of misclassification vary with the strategy used for inquiring participants. Open-ended questions may contribute to a worse recall of drug utilization, which was shown to be improved when drug names and indications or pictures as memory aids.

The way a questionnaire is structured is one of the several potential identified biases in a survey⁶⁸. It is known that even the method of contacting respondents and administering the questionnaire can influence data quality⁶⁰. According to *Choi et al*⁶⁸ questionnaires that are too long can induce fatigue among respondents and result in uniform and inaccurate answers. Avoiding open-ended questions is also referred in previous studies, as these can result in data with differential quality, and respondents are likely to be unwilling to take the time to answer them⁶⁸.

Influence of recall period in accuracy was also studied previously. *Kelly et al*⁶⁷ specifically evaluated the reliability of information over time. The study consisted in screening and evaluating two similar interviews regarding drug utilization diverging in time (one year or less) applied to the same in-hospital patients, comparing the percent

agreement between interviews (the percentage of the total in which the second response was the same as the first). Medications were reported more consistently when duration of use was prolonged and when the second interview followed the first by less than one year.

Biases from the order of the response choices, have been reported previously as well ⁶⁰. In self-administered questionnaires, respondents are likely to begin with the first response option presented (primacy effects) while in face-to-face or telephone interviews, respondents tend to begin processing the final option offered (recency effects). In a study addressing drug information, *De Almeida Neto, et al* ⁶⁹ also tested the hypothesis that differently ordered sequences of the same information about a drug can result in different judgments analysing two different surveys randomly distributed, one presenting the therapeutic benefits of a fictitious medication followed by potential adverse reactions and the other presenting potential adverse events followed by therapeutic benefits. The authors concluded that the order of presentation of information significantly affected judgement of the medication as the information displayed first had a larger affect on judgement.

Conclusion

Scientific work regarding methods for drug utilization data collection is scarce, particularly when addressing methods for elaborating drug utilization questionnaires in the general population. The existing evidence supports that recall of drug use was improved when drug names and indications or pictures were used as memory aids.

Table1. Details of the studies included in the systematic review.

Mitchell, 1986 ⁶²	
Objective:	To examine the effect of questionnaire design on the recall of drug use in pregnancy.
Study design:	The study consisted in a pilot interview study with three questions asking about drug use: one open-ended question, one asking about drug use for selected indications and one asking specifically for named drugs delivered to 532 women, followed by a case-control birth defects study with 5.435 participants (mothers of malformed infants) with questions asking for drugs by indication and than specifically named drugs.
Participants:	Pilot study: 532 women; Case-control: 5435 mothers of malformed infants
Questionnaire administration:	Personal interview
Questionnaire:	Pilot study: open-ended question, indication oriented question and drug oriented question; Case-control study: Indication oriented and drug oriented questions
Drugs studied:	Open-ended question: all drug classes Indication-oriented question: drugs used for 31 categories, such as headache/pain/backache/tension/strain/nerves, nausea/vomiting, high blood pressure, sleeping problems, fertility problems Drug-oriented questions: 17 specifically named drugs (including analgesics, psychotropics, diuretics and antiemetics).
Recall period:	Antenatal period, assessed in the first six months after delivery
Main results:	Pilot study: 13-45% of the drug used was reported drug use in response to the open-ended question; an additional 35-58% were founded in response to the question-listing indication; the remaining 20-35% reported only when the specific drug name was asked Case-control: drugs only reported when asked for the specific drug by name varied from 6% (Clomid *) to 40% (Darvon* and Seconal®) Mean percentage of respondents only when specific drug name was asked: 20-40%
Conclusions:	Recall of antenatal drug exposure varies according to how the mother is questioned. It is directly related to the specificity of the questions asked. Structured questions about indications and drug names are far more successful than are open-ended questions.

de Jong-van den Berg et al, 1993⁸³

Objective:	To compare reliability of information about drug therapy and pregnancy retrieved by interviewing patients with that distilled from pharmacy records. Different questionnaire structures were also compared.
Study design:	The interview consisted of a first open-ended question, extended with an indication oriented set of questions and then a set of specific drug-oriented questions. Data was also compared with pharmacy records.
Participants:	295 Dutch women who had delivered a born baby between 1 February and 15 June 1990, either at home or in hospital.
Questionnaire administration:	Personal interview
Questionnaire:	Open-ended question Indication oriented question («Have you used any medication or treatment during pregnancy for any of the following complaints?») Drug oriented question (a list of drugs was presented)
Drugs studied:	Open-ended question: all drugs Indication-oriented question: drugs for 24 different indications (eg. anaemia, cold and flu, diabetes mellitus, asthma, diarrhoea, fever) Drug-oriented question: list of 25 vitamin A, vitamin B, and vitamin D formulations and 16 laxatives.
Recall period:	Preceding pregnancy period, evaluated within 2 weeks after delivery
Main results:	79% of respondents admitted using at least one drug during pregnancy, and this number rose to 85% after the addition of indication-oriented questions and then to 88% after putting the drug-oriented questions. The most prominent rise was observed for the OTC drugs (the category in which vitamins and most laxatives belonged to) after the second set of queries with 45% of the women reporting the use of one or more OTC drugs. Agreement between the interview and the pharmacy data was 84% including the supplementary sets of questions.
Conclusions:	If drug consumption during pregnancy is evaluated by interview, one should not restrict oneself to open-ended questions but should include indication-oriented and, when appropriate, drug oriented questions.

Gmel et al, 1999⁶⁴

Objective:	To investigate the comparability of two questionnaires versions differing in the order of questions about the use of several medicines and herbal products and vitamins.
Study design:	In October 1996 the two versions of the questionnaires used for the First and Second Swiss Health Surveys were assigned randomly to a sample of 994 respondents (N1 = 537; N2 = 457).
Participants:	994 participants of the Swiss Health Survey.
Questionnaire administration:	Self-administered questionnaire.
Questionnaire:	<p>Version A presented first a question « Have you in the last 7 days taken any medicine or herbal products?» and the list of medicines was followed by herbal products and vitamins.</p> <p>In version B herbal products and vitamins were presented first followed by the question « Have you in the past 7 days taken any of these medicines?» and the same list of medicines afterwards.</p>
Drugs studied:	Several medicines (analgesics, antiasmatics, antirheumatics, laxatives, Ansiolytics, Hypnotics) and remedies (vitamins, herbal products)
Recall period:	Preceding 7 days.
Main results:	<p>For the groups of medicines asked (analgesics, antiasmatics, antirheumatics, laxatives, ansiolytics, hypnotics), the different questionnaire versions resulted in no significant differences ($p > 0.05$) in the prevalence of use.</p> <p>Differences were observed according to whether a skip question about the use of medicines in general precedes the questions on specific medicines. Version A yielded a higher prevalence of daily use of tonics and fortifiers (A vs. B: 7.4% vs. 4.8%; $p < 0.10$). Version B yielded a higher prevalence of daily use of vitamins (A vs. B: 9.9% vs. 5.1%, $p < 0.05$).</p>
Conclusions:	The difference between using a skip question separating herbal products from medicines seems to be relevant in the collection of data.

Klungel, 2000⁵²

Objective:	To assess the recall accuracy of questionnaire information on drug use obtained by open-ended questions and questions about the use of medications for specific indications, in comparison with pharmacy records
Study design:	Subjects were interviewed with five questions asked in sequence, to obtain information on drug use for specific indications and with one final open-ended question to assess drug use for any other condition. Questionnaire information was compared to pharmacy records from at least 90 days before the interview date from all community pharmacies in the same region. The study covered the period from 1987 to 1991.
Participants:	372 hypertensive subjects aged 20-59 years for whom questionnaire information and pharmacy records were available
Questionnaire administration:	Self-administered questionnaire filled at home.
Questionnaire:	Directed recall (5 questions): «Do you take antithrombotics? If yes, for which conditions?», «Do you currently take medications to lower blood pressure? If yes, which medications? », «Do you currently take medications to lower cholesterol? If yes, which medications? », «Do you have diabetes? If yes, do you use: a diet, tablets, injections or nothing? », «Do you currently take contraception pills? If yes, which brand? » Open-ended question: « Do you take any other medications that you have not yet mentioned? If yes, which medications?»
Drugs studied:	Direct recall: antithrombotics, antihypertensives, lipid lowering drugs, antidiabetics, oral contraceptives. Open-ended question: drugs for any other condition Drugs recalled with the open-ended question were grouped in: alimentary tract, dermatologicals, thyroid drugs, musculo-skeletal, psycholeptics, and other.
Recall period:	Current use
Main results:	71% of all drugs that were currently in use according to the pharmacy records were recalled through the questionnaire; 19% of the subjects mentioned one or more drugs that were not in use according to the pharmacy records and full agreement on current prescription drug use between both information sources was presented among 248 (67%) subjects. The sensitivity of recall of drugs in the questionnaire was much better for directed recall than for the open-ended question (88% vs. 41%, $p < 0.01$). Recall increased with the duration of drug use, both for the directed (use for < 3 months: 62.5%; use for 3-6 months: 75.1%; use for > 6 months: 92.3%) and the open ended question (use for < 3 months: 17.7%; use for 3-6 months: 42.9%; use for > 6 months: 55.2%), and with education, especially for the open ended question (low education: 41.0%; intermediate: 21.1%; high: 71.4%).
Conclusions:	Questionnaire structure might be of influence on the accuracy of recall of self-reported drug use. Recall sensitivity was higher for questions about drug use for specific indications than for an open-ended question.

Neutel, 2000²⁸

Objective:	To determine the relation between self-reported drug use categories (in the previous 30 days) and the actual specific drug products that the respondents state they are taking (in the previous two days).
Study design:	Participants were interviewed by telephone with two open-ended questions: one about self-reported drug use categories used in the previous 30 days and the other about specific drugs used in the in the previous 2 days.
Participants:	Respondents to the National Populational Health Survey in Canada (1996-1997), 62,588 adults (20 years of age or older).
Questionnaire administration:	Telephone interview.
Questionnaire:	Drug categories: « In the past month did you take any of the following medications? » (display drug categories) Specific drug product question: « What medications did you take over the last two days?» (display drug names)
Drugs studied:	Drug categories: 21 drug use categories combining 3 pairs of categories (insulin and oral diabetic drugs, antihypertensives ant diuretics, tranquilizers and sedatives) Specific drug product question comprising 26 ATC codes.
Recall period:	Previous 30 days (drug categories) Previous 2 days (drug names)
Main results:	From those who indicate taking specific antibiotics in the previous 2 days, 17.8% did not answered yes to the question about the antibiotic category referring to the previous month. Similarly 46.7% of the people who reported taking a narcotic analgesic in the previous 2 days had not reported taking drugs in the narcotic analgesic category in the previous month.
Conclusions:	Asking about specific drug names enhances accuracy better than asking for drug categories.

Kimmel, 2003 ⁶¹

Objective:	To estimate the degree to which use of medication lists and pictures improves recall of non-aspirin non-steroidal anti-inflammatory drugs (NANSAIDs) and to identify factors associated with enhanced recall from these memory aids,
Study design:	Participants were asked to recall any medications used for symptoms commonly treated with NANSAIDs, and then asked to look at a set of memory aids and to recall the use of those drugs. The recall of NANSAID use was considered to be enhanced by the memory aids if NANSAID use was reported only after review of the memory aids.
Participants:	This study was conducted as part of a case-control study designed to examine the effects of NANSAIDs on the risk of acute, first myocardial infarction. It included 1484 NANSAIDs users (cases and controls), aged 40 to 75 years,
Questionnaire administration:	Telephone interview. After an indication oriented question, participants were asked to refer to memory aids sent by mail in advance of interview. Memory aids included: a set of photographs of the most commonly used NANSAIDs (including 21 prescription and 11 non-prescription products), a list of 56 brand-name NANSAIDs and NANSAIDcontaining products for which pictures were not available, and a list of 24 generic drug names.
Questionnaire:	Indication-specific question: medications used for symptoms commonly treated with NANSAIDs (aches and pains, sore muscles, headaches, arthritis symptoms, gout, fever, cold or flu symptoms, and inflammation). Use of memory aids: participants were asked to look at the pictures and names of NANSAIDs while the names were read to them and to identify any of these medications used. If participants did not have the picture available, the entire list of NANSAIDs was read to them.
Drugs studied:	Non-aspirin non-steroidal anti-inflammatory drugs (NANSAIDs)
Recall period:	During the week prior to the index date (date of MI for cases and date of interview for controls).
Main results:	NANSAIDS were recalled by 90% (95%CI: 88.4%-91.5%) of the participants after the indication-specific question, and 6.3% (95%CI: 5.1%-7.4%) only recalled drug utilization after using memory aids. Several groups demonstrated enhanced recall following the memory aids: men (OR=1.73; 95% CI: 1.11-2.69), those not having their medication containers during the interview (OR=1.58; 95%CI: 1.03-2.42), users of non-prescription vs. prescription NANSAIDs (OR=2.28; 95%CI: 1.21-4.30), those using more than two other medications (OR 1.69; 95% CI: 1.06-2.69) and cases vs. controls (OR 1.90; 95% CI: 1.11-3.28). The ORs for cases vs. controls increased with increasing age. A higher proportion of cases had enhanced recall following the memory aids if their recall period was≤90 days versus>90 days (OR=5.07; 95% CI: 1.09-23.7).
Conclusions:	Reading of medication names with the availability of medication photographs may reduce recall bias in case control studies that rely in medication recall.

Ademi et al, 2007⁶⁶

Objective:	To compare 3 different measures of analgesic use in 1 study population over an 11-year period.
Study design:	Participants reported on their use of analgesics for pain during the past week (7 days) using 3 different measures simultaneously at baseline, 4 years, and 11 years of follow-up. By using 3 measures it was anticipated that more comprehensive information on the use of analgesics would be obtained, as there was no single "gold standard" available.
Participants:	Men (n=829) from a population based cohort.
Questionnaire administration:	Self-administered questionnaire (checked for missing information by a nurse, and patients were also asked to take all of their prescriptions with them to the examination).
Questionnaire:	Three questions: 1) "How often do you usually use analgesics?" 2) "For which of the following symptoms have you taken medicines during the past week (7 days)?"; a) headache, b) back or joint pain, and/or c) other pains. 3) "Which analgesics have you used during the past week (7 days) either prescribed by a physician or without prescription?"
Drugs studied:	Analgesics (NSAIDs, acetaminophen, opioids, and different combinations that include these substances). Low-dose aspirin and topical antirheumatics were not included in the analysis.
Recall period:	Preceding week (7 days)
Main results:	Prevalence at baseline (questions 1, 2 and 3): 12.3%, 13.5% and 17.4%; Prevalence at 4-year follow-up (questions 1, 2 and 3): 15.7%, 14.5%, 20.9% Prevalence at 11-year follow-up (questions 1, 2 and 3): 16.5%, 24.2%, 25.9%
Conclusions:	The measure being used influences the obtained prevalence of analgesic use. All 3 measures tested consistently throughout the course of the study. The best results were obtained by asking the respondents to name the medicines they had been using during the previous week.

Lunet, 2007⁶⁵

Objective:	To compare the recall of antimalarial drugs using two questionnaires differing in the order by which the answer options were presented.
Study design:	Clusters of participants were randomly assigned to one of the two questionnaire versions.
Participants:	504 University students from Maputo, Mozambique.
Questionnaire administration:	Self-administered questionnaire.
Questionnaire:	Differently ordered sequences of the same information: Version A: First drug was quinine, followed by Chloroquine, and the remaining drugs were ordered by decreasing frequency of utilization Version B: Less frequently used drugs came first, and quinine was placed at the end.
Drugs studied:	Antimalarials.
Recall period:	Questions referring to the treatment in the most recent malaria episode (when applicable).
Main results:	Significant differences for treatment using quinine (A vs. B: 19.5% vs. 11.6%, $p=0.006$) or artemisine/artesunate (A vs. B: 7.3% vs. 16.5%, $p=0.012$). The magnitude of the difference between versions A and B of the questionnaire was higher for subjects having had more than one malaria episode or when the last episode occurred longer before the date of interview.
Conclusions:	The structure of the questionnaire used to collect self-reported information about antimalarial treatment influences the recall, The first antimalarial drugs being presented first in the list of answer options were more likely to be selected. The results suggest that when more frequently used drugs are placed at the end of the list of answer options the report of drug utilization is more accurate

OR – Odds Ratio; 95%CI – 95% Confidence Interval.

**Effect of two different structures of questionnaire on recall
of drug utilization in a population of University Students**

Abstract

Introduction

Drug utilization data collected through questionnaires is commonly used in Epidemiological studies. However it is difficult to avoid variations in questionnaire structures that can affect data quality.

In this study we aim to compare the recall of medication use evaluated with two questionnaires differing in structure and length (long questionnaire including indication/drug specific questions vs. short questionnaire including one open ended question and several examples of indications and drugs).

Methods

Drug utilization was assessed in two alternative versions of a questionnaire (version A was 4 pages long and included separate questions, with the respective examples of specific drugs, for each of 13 group of medicines; version B was one page long and included a single open-ended question to cover overall drug consumption, preceded by a small text including the same examples that were provided in each of the questions from version A). Questionnaires A or B were randomly assigned to each of the 32 classes in a private University in Maputo, Mozambique. Within each classroom all subjects received the same questionnaire version (A: 233 participants; B: 276 participants).

Results

Among these 509 subjects, 343 (67, 4%) used at least one drug in the previous month. From the drugs listed, the most commonly reported was the analgesic group, with almost half of the population reporting its use (236 (46.4%)). Other commonly used drugs were vitamins (66 (13%)) and anti-histamines (68 (13.4%)). The least used drugs were antimalarials (8 (1.6%)), antitussives (8 (1.6%)) and antiasthmatics (17 (3.3%)). Population in questionnaire A reported drug utilization more frequently than in questionnaire B, however these results were only statistically significant for antibiotics

(14.6% vs 6.9%, $p= 0.001$), antifungals (9.4% vs 4.0%, $p=0.013$) and antacids (8.6% vs 3.6%, $p=0.024$)

Conclusions

Drug recall was similar in both versions of the questionnaires, both for the most and the least commonly used drugs. Also the structure of the questionnaire used did not influence recall when asking for chronically used drugs. Differences were noticed for not so commonly used groups of drugs.

It is possible to create a reliable questionnaire concerning overall drug utilization without being an overextended survey. Ideally, the creation of a well designed, validated questionnaire should be available for researchers in order to employ similar methods that could be directly comparable in different settings.

Introduction

Self-reported data is a common source of drug exposure information⁵² and in many settings it is the only method available to characterize drug use³.

Modes of data collection by questionnaire may differ in several ways, including the methods of contacting respondents, the medium of delivering the questionnaire and the administration of the questions⁶⁰, which may be reflected in the reliability and validity of the method^{60,68}. Regarding drug utilization, even minor changes in question wording⁶⁸, question^{64,65} or response⁶² order or format can result in misclassification of the exposure. Studies addressing the effect of questionnaire design on the recall of pharmacological treatments are unanimous in showing that indication or drug oriented questions yield higher prevalence of drug utilization than open-ended questions^{28,52,61-63,66}. However obtaining data related to various drug categories frequently requires extensive questionnaires including separate questions for each of the main pharmaceutical groups. The use of large number of questions for this purpose may not be possible or desirable, as it may increase substantially the size of the questionnaire and lead to poor acceptability and compliance by the participants. A shorter questionnaire may be more limited in its ability to characterize drug utilization in its full extent, but has obvious benefits in terms of a reduced burden over the respondent and costs of the investigation^{70,71}.

We hypothesized that a single item questionnaire complemented with examples of the indications and medicines expected to be more frequent in the studied population could yield similar prevalence estimates on drug utilization as an extended multi-item questionnaire. Therefore, we aimed to compare the recall using two questionnaires differing in structure and length (long questionnaire including indication/drug specific questions vs. short questionnaire including one open ended question and several examples of indications and drugs).

Methods

This investigation was performed in students enrolled at a private University in Maputo in 2006. Socio-demographic information and regarding the drugs used in the previous month (when applicable) was collected using a self-administered questionnaire applied in all diurnal classes, with the consent of the teachers. Ten students (1.9%) refused to participate (1.6% of those receiving questionnaire A and 2.1% of those receiving questionnaire B) and 509 were evaluated, approximately 50% of the total number of students in the institution in diurnal classes.

Two alternative versions (A and B) of the questionnaire, which differed in the question structure and length, were used to collect information. Both questionnaire versions started with the same close-ended question “*Did you use some medication in the last month (including tablets, capsules, injections, ointments, ovules, syrups, etc.)?*”, and provided similar general instructions to the participants. Questionnaire A (Annex 1) was 4 pages long and included separate questions, with the respective examples of specific drugs, for each of 13 group of medicines («Medications for treatment of pain and inflammation (*e.g.*, Paracetamol, Voltaren®/diclofenac, ibuprofen, etc.), Medications for treatment of flu or cold (*e.g.*, Cêgripe®, Constipal®, Corenza® C), Antibiotics (*e.g.*, Amoxicillin, tetracycline, co-trimoxazol, metronidazol, etc.), Antifungics for treatment of infections (*e.g.*, Canesten®, Clotrimazol®, Quadriдерme®, Nalbix®, etc.), Antimalarials (*e.g.*, artemisine + fansidar, etc.), anti-parasitics (*e.g.*, albendazol, mebendazol, etc.), Vitamins and minerals (*e.g.*, multivitamins, complex B, ferrous salt, C vitamine, etc.), antiasthmatics (*e.g.*, salbutamol/Ventilan®, aminofiline, becometazol, prednisolona, etc.), anti-hystaminics (*e.g.*, clorfeniramine, loratidine, Claratine®, etc.), oral contraceptives/«pill» (*e.g.*, Diane® 35, Microginon®, etc.), antitussives and/or expecturants (*e.g.*, Benilyn®, Diacol®, Benetussin®, Tosseque®, sodium benzoate, etc.), or medications for gastric problems (*e.g.*, omeprazol, cimetidine, ranitidine, ENO®-fruit

salts, hydroxide aluminum, Rennie®, Kompensan®, etc.). Subjects were asked to complete an open-ended table for each group, with the following information for each drug: brand or generic name, duration of treatment, self-medication (including pharmacy-counselled) versus physician-prescription, and intended purpose. The pharmacological groups for which specific questions were performed in questionnaire A and the examples given to the participants were selected according to the results of a previous survey conducted in the same setting ⁷². Questionnaire B (Annex 2) was one page long and included a single open-ended question to cover overall drug consumption, preceded by a small text including the same examples that were provided in each of the questions from questionnaire A. Subjects were asked to complete an open-ended table similar to the ones described for questionnaire A.

Each medicine mentioned in questionnaires A or B was coded to the second level of classification (therapeutic subgroup) of the WHO Anatomical Therapeutic Chemical classification (ATC) ⁷³. The groups considered for the analyses and respective ATC subgroups were: Analgesics (including ATC M01 – Anti-inflammatory and anti-rheumatic drugs, non steroids, N02 – Analgesics, B01 – Antitrombotic agents); anti-histamines (ATC R06 – Antihistamines for systemic use); Antitussives (ATC R05 – Cough and cold preparations); Antacids (ATC A02 – Drugs for acid related disorders); Antibiotics (ATC J01 – Antibacterials for systemic use); Antifungals (ATC D01 – Antifungals for dermatological use; G01 – Gynecological antiinfectives and antiseptics; D07 – Corticosteroids, dermatological preparations, combinations with antibiotics, J02 – Antimicrotics for systemic use); Antiasthmatics (R03 – Drugs for obstructive airway diseases, H02 – CCT for systemic use; Antiparasitics (P01(except P01B) – Antiprotozoals; P02 – Anthelmintics); Vitamins (ATC A11 – Vitamins, B03 – Antianemic preparations); Antimalarials (ATC P01B – Antimalarials); Hormonal contraceptives for systemic use (ATC G03 – Sex hormones and modulators of the

genital system; L02 – Endocrine Therapy); Others (including all the drugs not included in the previously described groups).

To test hypothesis that the structure of the questionnaires yielded the same prevalence of drug utilization the two questionnaire versions were randomly assigned to each of the 32 diurnal classes using a list of random numbers generated with the software EPIInfo, version 6.04d⁷⁴. Questionnaires A and B were assigned to 14 and 18 classes each. Within each classroom all subjects received the same questionnaire version (A: 233 subjects; B: 276 subjects).

This sample allows for the detection of differences in the estimates of the two questionnaires with a power of 80%, for a 95% confidence level, when the magnitude of the difference corresponds to a risk ratio of two, and the proportion of drug use is above 10%, considering design effect as high as 1.15 (which would be obtained for an average cluster size of 15 and an intra-cluster correlation coefficient of 0.01)^{75,76}.

The two groups (questionnaire A and questionnaire B) were compared, regarding socio-demographic characteristics, medication used during the previous month, through logistic regression with robust standard errors (allowing for clustering by classroom)⁷⁷. All the tables present P-values corresponding to comparisons with no adjustment of covariates. Data were analyzed using STATA®, version 9.2.

The National Ethics Committee of Mozambique approved the study protocol. Students were asked to read an informed consent form stating the general objectives of the study and data collection methods, in agreement with the *Declaration of Helsinki*. Only students who signed the informed consent form were allowed to participate and were asked to complete the questionnaire.

Results

There were no statistically significant differences in the baseline evaluation of the participants answering questionnaires A or B, regarding sociodemographic

characteristics and the proportion of users of at least one medicine in the previous month (67.4% vs. 67.4%, $P=0.999$) (Table 1).

The median number of medicines used per person among drug users was higher among subjects receiving questionnaire A (2 vs. 1) as well as the proportion of participants reporting the use of two or more drugs (66.2%vs. 43.0%, $P<0.001$). Also, the median number of different pharmacological groups to which the drugs used by each subjects belong (2 vs. 1) and the proportion of participants reporting the use of drugs from two or more pharmacological groups (60.5%vs. 34.4%, $P<0.001$) was higher among those filling questionnaire A.

Table 1 – Baseline characteristics of participants evaluated with questionnaires A (14 classrooms, 233 subjects) and B (18 classrooms, 276 subjects).

	Number of subjects*	Questionnaire		P
		A n (%)	B n (%)	
Age (% above 20)	489	101 (44.9)	103 (39.0)	0.557
Sex (% male)	497	80 (35.2)	104 (38.5)	0.728
Study area (% health related)	509	77 (33.0)	88 (31.9)	0.949
Grade (% above 2 nd grade)	509	133 (57.1)	111 (40.2)	0.404
Users of at least one medicine during the previous month	509	157 (67.4)	186 (67.4)	0.999

* The number of subjects may differ from 509 due to missing data.

Participants answering questionnaire A recalled more frequently the use of antibiotics (6.9% vs. 14.6%, $p=0.001$), antifungals (4.0% vs. 9.4%, $p=0.013$); antiparasitics (1.8% vs. 5.6 %, $p=0.031$) and antacids (3.6% vs. 8.6%, $p=0.024$), but no statistically significant differences were observed for the remaining drug groups.

Table 2 – Medication used during the previous month, according to the type of questionnaire (n= 509).

	Questionnaire		P
	A n (%)	B n (%)	
Analgesics	113 (48.5)	123 (44.6)	0.509
Antibiotics	34 (14.6)	19 (6.9)	0.001
Antifungals	22 (9.4)	11 (4.0)	0.013
Antiparasitics	13 (5.6)	5 (1.8)	0.031
Antimalarials	3 (1.3)	5 (1.8)	0.690
Vitamins	38 (16.3)	28 (10.1)	0.118
Antiasthmatics	7 (3.0)	10 (3.6)	0.666
Anti-histamines	34 (14.6)	34 (12.3)	0.362
Contraceptives*	14 (9.5)	14 (8.4)	0.742
Antitussives	6 (2.6)	2 (0.7)	0.118
Antacids	20 (8.6)	10 (3.6)	0.024
Other drugs	22 (8.0)	18 (7.7)	0.922

* Only women data

When data were analysed separately for males and females, the relation between the prevalence of drug use remained essentially the same for both sexes (Table 3).

Table 3 – Medication used during the previous month, according to the type of questionnaire, in women and in men.

	Women (n=313)			Men (n=184)		
	Questionnaire		P	Questionnaire		P
	A	B		A	B	
	n (%)	n (%)		n (%)	n (%)	
Analgesics	75 (51.0)	86 (51.8)	0.916	36 (45.0)	36 (34.6)	0.074
Antibiotics	21 (14.3)	12 (7.2)	0.007	11 (13.8)	7 (6.7)	0.186
Antifungals	14 (9.5)	7 (4.2)	0.013	7 (8.8)	4 (3.8)	0.115
Antiparasitics	12 (8.2)	3 (1.8)	0.002	1 (1.2)	2 (1.9)	0.685
Antimalarials	2 (1.4)	5 (3.0)	0.445	1 (1.2)	0 (0.0)	---
Vitamins	28 (19.0)	22 (13.2)	0.282	9 (11.2)	5 (4.8)	0.111
Antiasthmatics	6 (4.1)	6 (3.6)	0.812	1 (1.2)	4 (3.8)	0.325
Anti-histamines	23 (15.6)	22 (13.2)	0.541	10 (12.5)	12 (11.5)	0.802
Antitussives	3 (2.0)	1 (0.6)	0.268	3 (3.8)	1 (1.0)	0.220
Antacids	17 (11.6)	8 (4.8)	0.048	3 (3.8)	2 (1.9)	0.322
Other drugs	13 (8.8)	10 (6.0)	0.316	3 (3.8)	4 (3.8)	0.977

The proportion of subjects not providing information regarding the duration of the treatments previously reported differed across pharmacological groups, but tended to be much higher among participants answering questionnaire B.

The duration of treatment reported by the participants ranged from 1 day for antimalarials and 2 days for analgesics (questionnaire B) to 1 months for oral contraceptives and 15 days for antiasthmatics (questionnaire B).

Table 4 – Medication used during the previous month, according to the type of questionnaire, in women and in men.

	Missing information regarding duration of treatment n (%)		Median duration of treatment (days)	
	Questionnaire		Questionnaire	
	A	B	A	B
Analgesics	10 (8.8)	25 (20.3)	3	2
Antibiotics	2 (5.9)	4 (21.0)	7	7
Antifungals	1 (4.5)	4 (36.4)	14	7
Antiparasitics	2 (15.4)	0 (0.0)	3	3
Antimalarials	0 (0.0)	2 (40.0)	3.5	1
Vitamins	3 (7.9)	7 (25.0)	15	7
Antiasthmatics	0 (0.0)	3 (30.0)	3.5	15
Anti-histamines	4 (11.8)	14 (41.2)	4	3
Contraceptives*	2 (14.3)	0 (0.0)	30	30
Antitussives	6 (100.0)	2 (100.0)	5	10.5
Antacids	1 (5.0)	2 (20.0)	3	4.5

* only women data

Discussion

The more detailed version of the questionnaire, with specific questions for each drug group, yielded a significantly higher prevalence of use of antibiotics, antifungals, antiparasitics and antacids. For the remaining drug groups the recall was similar in both structures of the questionnaires, for both the most and the least commonly used drugs, for chronic and acute conditions. Participants receiving the questionnaire version relying on a single open-ended question tended to provide less complete information regarding the duration of the treatments.

Although we approached students in all diurnal and most nocturnal classes and the proportion of refusals was low, information was obtained from only half of the institution's students. Females resulted overrepresented in our sample (63.0% vs. 37.0% enrolled in the university). In the present methodological approach data was collected at the campus premises, leaving absent students unsampled. Therefore the «Healthy worker effect» could account for a selection bias as those less fit are more prone for any type of drug use. Although the evaluated sample does not adequately represent the university population, and even less to the Mozambican population, that is not expected to compromise internal validity, but generalisation to less educated populations may not be possible.

A concern when using a large questionnaire such as version A is the burden that it imposes to the participant by requiring a large amount of time to answer the questions, which may result in a larger proportion of refusals and in missing data among the respondents. In our study was not possible to quantify the time taken by the participants to fill each of the questionnaire versions, but the proportion of refusals was similar for both questionnaire versions. Regarding the completeness of the answers, the proportion of subjects with missing information about the duration of treatment was even lower among those receiving questionnaire A.

No records were available to check the reported drug utilization against the prescribed and non-prescribed drug data, and therefore we did not have a gold standard to allow inferences about the absolute validity of exposure recall using questionnaires A or B, but the design used for questionnaire A is expected to provide more accurate estimates of drug utilization^{52,63}.

Some published studies indicate that the prevalence rates when dealing with medicines data based on analysis of questionnaires are more reliable than information retrieved from medical or pharmacy records, specially by assessing over-the-counter drugs and medication misuse^{54,55,78-80}. Additionally self-administration of questionnaires

can increase respondent's willingness to disclose sensitive information, compared with face-to-face or telephone interviews, leading to higher levels of reporting⁶⁰.

Ademi et al⁶⁶ had different results compared to ours regarding analgesics. In that study, considering asking for drug categories, drug indications and drug names, the highest prevalence was yielded for drug names. We didn't find this difference. However this could be caused by the high prevalence of analgesic intake in our population (46.4% in our study vs. 17.4% in the study by Ademi et al).

For antibiotics and antifungals the estimated prevalence differed between the two questionnaire structures. This was also noted by Neutel et al²⁸ who observed that antibiotics were better recalled when asked by specific name rather than by category only. Our study did not find differences between the two questionnaire versions when assessing antimalarials, which may be explained by the fact that malaria is a severe disease very frequent in this setting.

We also found that a substantial proportion of students obtained drugs from sources other than the prescribing physicians. This finding has implications for studies that rely on doctor-generated or pharmacy-based prescription records, whether recorded on paper or computer, in addition to the concern that such information includes false positive «exposures» (prescriptions issued or filled but not consumed). Our findings suggest that these data sources may also include an appreciable number of false negative exposures (drugs consumed but obtained from misidentified sources).

Conclusion

A standardized way of asking questions on drug use in large population-based studies does not seem to be commonly used. To avoid recall bias it would be important to pay more attention to the structure of questions on these surveys. It is possible to create a reliable questionnaire concerning overall drug utilization with no need for an overextended survey. Ideally, the creation of a well designed, validated questionnaire

concerning overall drug use should be available for researchers in order to employ similar methods that could be directly comparable in different settings.

Annex 1. Questionnaire A

1. Did you use some medication in the last month (including tablets, capsules, injections, ointments, ovules, syrups, etc.)?

0 no 1 yes

If you answered no, go to question 15 ((at the end of the page).

If you answer yes, please go to the next question.

Please fill in the next tables according to this example:

Name of the medicine or drug	Duration of treatment (in days)	Medical indication (yes or no)	Reason for using
Diane35	Everyday	yes	Prevent Pregnancy
Vitamins and minerals	± 15 days	No	Fatigue due to exams
salbutamol	SOS/urgency	Yes	Asthma
Canesten (cream)	15 days	No	Infection
Artemisinine+fansidar	Taken once	No	Malaria

If you don't remember the medication, please describe the type of medication and what it is used for.

If you only know how to answer to part of the questions that we are asking you, please answer to those that you know how to answer (please leave what you can't or don't remember in blank)

2. In the last month did you use some medication (tablets, capsules, injections, creams, syrups) for treatment of pain or inflammation (eg: paracetamol, voltaren/diclofenac, ibuprofen, etc.)?

0 no 1 yes

If you answered no, please go to question 3.

If you answered yes, please fill in the next table with the medication(s) that you used.

Name of medication or drug	Duration of treatment (in days)	Medical indication (yes or no)	Reason for using

Annex 2. Questionnaire B

1. Did you use some medication in the last month (including tablets, capsules, injections, ointments, ovules, syrups, etc.)?

0 no 1 yes

If you answered no, go to question 2 (at the end of the page).

If you answer yes, please fill in the table below with the medication that you used in the last month, according to the example:

To better remind you, here are some examples of medications: Medications for treatment of pain or inflammation (eg. paracetamol, voltaren/diclofenac, ibuprofen, etc.); Medications for treatment of flu or cold (eg. Cégripe, Constipal, Corenza C, etc); Antibiotics (eg. amoxicillin, tetracycline, cotrimoxazole, metronidazole, etc.), antifungals for treatment of infections (eg. Canesten, clotrimazole, Quadriдерme, Nalbix, etc.); antimalarials (eg. artemisinine+fansidar, etc.); antiparasitics (eg. albendazole, mebendazole, etc.); Vitamins and minerals (eg. multivitamins, complex B, ferrous salt, vitamin C, etc.); antiasthmatics (eg. salbutamol/Ventilan, aminofilin, beclomethasone, prednisolone, etc) antihistamines (eg. clorfeniramin, loratadine, claritin, etc.); oral contraceptives/"pill" (eg. Diane 35, Microginon, etc.); antitussives and/or expecturants (eg. Benilyn, Diacol, Benetussin, Tosseque, sodium benzoate, etc.); or medications for gastric problems (eg. omeprazol, cimetidine, ranitidine, ENO-fruit salts, hydroxide aluminium, Rennie, Kompensan, etc.)

If you don't remember the medication, please describe the type of medication and what it is used for.

If you only know how to answer to part of the questions that we are asking you, please answer to those that you know how to answer (please leave what you can't or don't remember in blank)

	Name of the medicine	Duration of treatment	Medical indication	Reason for using
example	Diane35	Everyday	Yes	Prevent Pregnancy
example	Vitamins and minerals	± 15 days	No	Fatigue due to exams
example	Erythromycine	8 days	Yes	Infection
example	Canesten (cream)	15 days	No	Infection
a)				
b)				
c)				
d)				
e)				

Abstract and Conclusions

Abstract

We aimed to address the relation between questionnaire characteristics and the recall of pharmacological treatments by participants in drug utilization studies. To accomplish our objectives, we performed studies using different designs: a systematic review and a cross-sectional analysis.

Paper I - Questionnaire design and the recall of pharmacological treatments: A Systematic Review

We reviewed systematically the published evidence on the effect of questionnaire design on the recall of pharmacological treatments. The searches returned 3069 potentially relevant articles. After review of the titles and removal of duplicates, 747 abstracts were read. 52 articles were selected for further evaluation and nine were included in the systematic review. Overall, recall was increased in 6, 3 to 47% when specific drug names or indications were asked (with or without memory aids) rather than an open-ended question, and in 8, 55% when drug was presented first instead of last. Mean enhanced recall also increased in 14, 4% for drug name rather than drug category.

Paper II - Effect of two different structures of questionnaire on recall of drug utilization in a population of University Students

In this study we evaluated the effect on recall among two different structures of medication questionnaires diverging only in the item formats. Drug utilization was assessed in two alternative versions (A and B) of a questionnaire, which differed only by the question structure (version A: groups of medicines were presented as separate questions, displayed in 13 different items; Version B: the same groups of medicines were presented as one open-ended question). Questionnaires A or B were randomly assigned to each of the 32 classes in a private University in Maputo, Mozambique. Within each classroom all subjects received the same questionnaire version, and a

similar number of participants fulfilled questionnaires A (n=233) and B (n=276). Population in questionnaire A reported drug utilization more frequently than in questionnaire B, however these results were only statistically significant for antibiotics (14.6% vs 6.9%, p= 0.001), antifungals (9.4% vs 4.0%, p=0.013) and antacids (8.6% vs 3.6%, p=0.024).

Conclusions

The main conclusions of these studies were:

Paper I - Scientific work regarding methods for drug utilization data collection is scarce, particularly when addressing methods for elaborating drug utilization questionnaires in the general population. It is important to avoid using open-ended questions, and rely more in drug names and indications or even pictures as memory aids than on drug categories, and if the most commonly used drugs are placed last there is a better probability of improving recall.

Paper II - Drug recall was similar in both versions of the questionnaires, both for the most and the least commonly used drugs. Also the structure of the questionnaire used did not influence recall when asking for chronically used drugs. Differences were noticed for not so commonly used groups of drugs.

It is possible to create a reliable questionnaire concerning overall drug utilization without being an overextended survey. Ideally, the creation of a well designed, validated questionnaire should be available for researchers in order to employ similar methods that could be directly comparable in different settings.

The use of computerized databases has greatly facilitated the study of drug utilization. Although useful, most of these databases are far from ideal, as they have been set up mainly for administrative purposes, such as reimbursement. But existing

medical and pharmaceutical databases, with all their described limitations, will continue to be the main resources for these drug utilization studies. Despite this, the search must continue for simple and relatively inexpensive methods for conducting descriptive studies of drug utilization and effective intervention strategies that may contribute to the optimization of drug therapy. Population-based questionnaires are a reliable source of drug utilization information and could be such a method, if recall bias was decreased to a minimum.

Future Perspectives

The study of drug utilization is an evolving field. The use of large computerized databases that allow the linkage of drug utilization data to diagnosis, albeit subject to some inherent limitations, is contributing to expand this area of study.

Drug utilization studies have been having an increasing importance in pharmacoepidemiology by means of bridging more closely to other areas:

Public health

From a **public health** perspective, the differences observed in national and international patterns of drug utilization require much further study. Many strategies aimed at modifying prescribing behaviours have been proposed and adopted. Several studies have demonstrated the efficacy of face-to-face methods in improving drug prescribing by identifying physicians who were prescribing drugs assessed as inappropriate and targeting for educational or information activities 81-83

However, drug utilization review programs as well as definition to what degree and which determinants of inappropriate prescribing are susceptible to modification and what might be an appropriate mix of interventions to achieve optimal impact merit further rigorous study.

Pharmacovigilance

Some of the actual existing databases have been developed primarily for drug safety studies (**Tayside Medicines Monitoring Unit (MEMO)** and the **General Practice Research Database (GPRD)** in the United Kingdom)⁴⁰. Pharmacovigilance plans require extend safety knowledge, in order to investigate potential drug-drug interactions and signal detection of adverse drug reactions. Drug utilization data can be used to perform screening for patients who may be at increased risk for drug-induced illnesses, often by use of concomitant drugs, abuse or overuse of drugs.

New registers offer countless possibilities for studying drug use among different groups of the society, but there is still a lot to achieve⁷.

It is also important to evaluate the paediatric population, since many medicines prescribed for children are given «off-label» and surveillance of natural non-registered products, such as herbal medicines in the general population is also needed.

Pharmacoeconomics

Drug utilization reviews can be used for the improvement of medical care and cost-containment, and are useful for measuring or comparing the economic impact of drug use in the population. By identifying adherence to guidelines in the current use of medicines, it is possible to reduce drugs expenditure and improve the allocation of the limited resources available, when the chosen drugs are not usually the most cost-effective.

Eco Pharmacovigilance

Pharmaceuticals are environment pollutants. It is important to observe the differences in national and international patterns of drug utilization in order to address and minimize the environmental impact of pharmaceuticals whilst continuing to deliver patient benefit.

Pharmacogenetics

Trying to assess genetic mechanisms related to drug safety issues is also a challenge for drug utilization studies, while comparing consumers' characteristics and linking it to the benefit and risk of drugs.

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