

Availability and quality of data on drug policy and management of access to reimbursed medicinal products in the United Kingdom, Denmark, Germany, Italy and Poland

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Abstract

Objectives: To perform a systematic review, and to verify and define deficiencies in literature data on drug policy and management of access to reimbursed medicinal products in the United Kingdom, Denmark, Germany, Italy and Poland as a source of information intended to be used by government authorities in the decision-making process.

Methods: A systematic review was conducted through database search of Medline, SCOPUS, Embase and Cochrane Library, supplemented by non-systematic review. The quality of the identified literature was critically appraised.

Results: Information necessary to develop a knowledge base was outline from 121 papers identified through database search. 0.83% of all publications were rated high in all of the assessed categories, i.e. were identified to represent high levels of consistency, coherence, strength and methodological quality.

Conclusions: In the policy decision-making process, concise recommendations based on validated data are more than needed. It is vital to rely on scientific evidence and avoid reports based on simple exchange of information or presenting single-source or unconfirmed data, including expert's opinion.

Key words: data availability, decision-making process, methodology assessment, quality

Słowa kluczowe: dostępność danych, jakość, ocena metodologii, proces decyzyjny

Introduction

The objective of this paper was to perform a systematic review, and to verify and define deficiencies in literature data on drug policy and access management to reimbursed medicinal products in the United Kingdom, Denmark, Germany, Italy and Poland. Found publications should serve as a source of information intended to be used in the decision-making process by government authorities who should rely on scientific evidence and avoid reports based on simple exchange of information between government institutions as well as reports and publications, based on single or random/unconfirmed sources of information. According to conversations with a number of officials from the Polish Ministry of Health and own conclusions from the review of official reports [1–5], we arrived at the hypothesis that the proper methodology of systematic literature review and assessment of the quality of the identified papers and the obtained data is not so common as expected previously. As a result, this work is intended to investigate and outline the possible bias which could originate from using and relying on data sources other than those derived from proper scientific methodology for identifying literature data eligible to be included in official reports. Our hypothesis is mainly based on a common practice of insufficient or missing description of methodology defining the inclusion criteria for publications quoted such reports [1–5]. Despite the fact that systematic review involving quality assessment of the literature data has been widely recognized as methodological standard, it is still uncommon in institutional practice.

In order to estimate the extent to which data from poor-quality publications are in fact used, and the chance of finding high-quality article without employing the widely recognized methodology of systematic review and assessing literature data quality, we evaluated the quality of a large number of literature data addressing specific areas of drug policy and management of access to reimbursed medicinal products in the United Kingdom, Denmark, Germany, Italy and Poland, on the assumption that otherwise some biased conclusions can be arrived at.

This work was part of International Research Project on Financing Quality in Healthcare – InterQuality, Work Package 3, whose objective is to validate pharmaceutical benefit financing (pricing and reimbursement) models used in:

1. Tax or social health insurance systems, relying mainly on official drug prices, government-regulated distribution mark-ups, and pharmaceutical care rewards.
2. Private or mixed health insurance systems, relying mainly on market forces and used in managed competition framework to set drug prices, manage distribution costs, and set pharmaceutical care incentives.

Methods

Work outline

Firstly, on the basis of our knowledge and multiple consultations with various experts, we prepared a list of issues and problematic questions to be answered during

the data research. Secondly, in order to assess availability of data and collect the intended set of information, we performed a standard systematic review and developed a bibliography list of all relevant full-text papers included in the review, extracting the most important data into pre-defined tables. On conclusion of the systematic review, it was concluded that some necessary information and data were still missing and therefore a “non-systematic review” was carried out to improve data availability and quality. The non-systematic review consisted of manual literature search, tracing the relevant references to selected full texts, and consulting experts in the areas of interest about other relevant papers they are familiar with. The collected information and data were extracted to the same pre-defined table used in the systematic review.

Finally, having collected all papers, the quality of various types of publications was assessed using three checklists which were considered relevant for the design of specific papers to avoid possible mistakes in the application of checklists. In addition to quality assessment of publication designs, the actual value of the publications was scrutinised and the assessment results were entered in the tables.

Figure 1 presents the workflow diagram.

Developing lists of issues and problematic questions

The first methodology used in the development of a list of relevant topics was the Focus Group Discussion (FGD) – the most popular qualitative technique demonstrated to be valuable in many scientific and commercial applications, where confrontation and mutual stimulation of respondents is expected to deepen understanding of the subject discussed. FGD advantage is that it not only accumulates participants’ expertise, but it also can produce synergy between them: common understanding of the subject is created as group members start to stimulate and to enlighten each other, sharing their experience. On the other hand, the commonly recognized disadvantage of FGD is the “group effect” attributed to the natural pressures towards conformity.

The second methodology was Delphi Panel Method – “a structured method of eliciting expert judgment that is particularly useful as a tool to achieve consensus of opinion when the decisive factors are subjective”. Delphi procedure involves a series of interrogations in which anonymous responses of group members are submitted to the group for comment until consensus is reached. The WP3 research team, being a group experienced in the healthcare sector and representing a range of environments and perspectives, acted as the expert panel and developed the list of relevant topics and questions based on the outcomes of FGDs and the Delphi panel. The list was validated by a group of experts from other partner countries at the InterQuality meeting in Catania on 25 May 2012. The list was the basis for inclusion of publications as part of the systematic review.

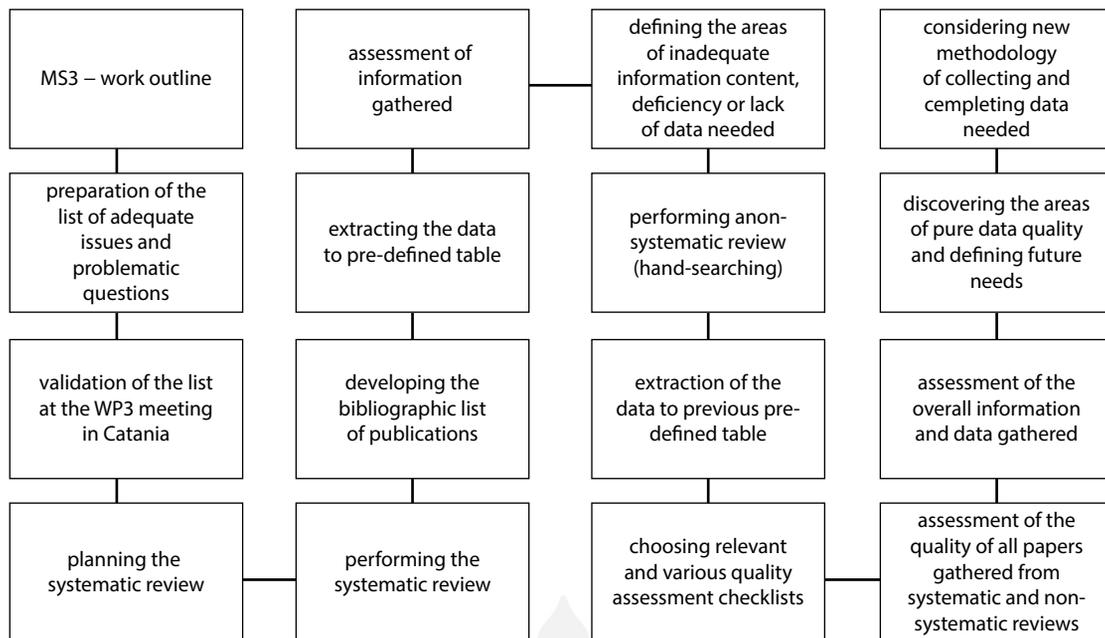


Figure 1. Work outline diagram.

Source: Own elaboration.

Methodology of systematic review

Systematic literature review was conducted through database search of Medline, SCOPUS, Embase and Cochrane Library. A search strategy (**Table I** and **II**) was established to identify the available literature data on topics defined during FGDs and the Delphi panel. A number of synonyms was identified for each phrase. “Wild cards” were employed to broaden the search, including different forms of key words. Key words were combined using the Boolean system. The review involved specific limitations attributed to the need to make room for economic studies.

The first step in selecting publications was the “title/abstract screening”. The review was performed by eight members of the WP3 team. Inclusion criteria were as follows:

1. Addressing one of the previously defined areas of interest (healthcare systems as a framework for drug policy, pricing and reimbursement, and co-payment).
2. Description of problems from the system-wide and multiple-issue point of view.

To account for the economic studies, the inclusion criteria by PICOTS (population, intervention, comparator, outcomes, time, setting) were implemented, save for some limitations:

- Population: any individuals or organizations receiving or providing the intervention/policy in the topic of our interest.
- Intervention: if relevant, initiatives to improve quality, equity, safety and efficiency of the intervention/policy in the topic of our interest.
- Comparator: if relevant, of available, alternative initiative to those listed in the Intervention.

- Outcome: outcomes of interest in the framework of InterQuality Project: quality, costs, efficiency and equity in the framework of process, structure and outcome.
- Time: review was limited to years 2002–2012.
- Settings: Intervention/policy in areas of our interest (healthcare systems as a framework for drug policy, pricing and reimbursement, and co-payment). RCTs were excluded.

On exclusion of irrelevant publications in the title/abstract screening, the full-text review was performed. Publications unavailable in full text in English or Polish were also excluded. Each publication was reviewed by two reviewers to check if all the inclusion criteria were met. Where any disputes over the inclusion arose, the final decision was based on consensus. If the consensus failed to be reached, the decision was made by the scientific coordinator of the review. Finally, complete bibliography lists of the identified full-text publications were prepared.

The most important data from the included papers were extracted into the predefined tables and short descriptions were entered into tables for identification. At this point, the areas of insufficient data, inadequate information content or deficiencies in any important data were identified for further research under the “non-systematic review”.

Methodology of manual search

An additional “hand-search” of literature was performed. References were traced of full texts identified in the systematic review and included in the bibliography

No	Query
#1	generic OR nonproprietary OR "Drugs, Generic"[Mesh]
#2	statins OR "Hydroxymethylglutaryl-CoA Reductase Inhibitors"[Mesh] OR simvastatin OR rosuvastatin OR atorvastatin
#3	prescription OR substitution OR switching OR replacing OR "Drug Substitution"[Mesh] OR "preferred drug"
#4	#1 AND #2 AND #3
#5	innovative OR innovation
#6	medicine OR drug OR pharmac*
#7	#5 AND #6
#8	"new entity" OR "new drug"
#9	#7 OR #8
#10	"e-prescribing" OR „electronic prescribing" OR "e-prescription" OR "electronic prescription" OR "electronic medical record" OR "computerized medical record" OR "electronic health record" OR "computerized health record" OR "electronic drug monitoring" OR "computerized drug monitoring" OR "online adjudication" OR "pharmacy claims" OR "DUR" OR "drug utilization review" OR "PBM" OR "pharmacy benefit management"
#11	transparency OR access OR accessibility OR affordability
#12	#6 AND #11
#13	"personalised medicine" OR "personalized medicine" OR "targeted therapy"
#14	#4 OR #9 OR #10 OR #12 OR #13
#15	"market share" OR price OR incentives OR "patient satisfaction" OR cost OR spendings OR (financing AND (model OR system)) OR (principal AND agent) OR agent OR distribution OR competitiveness OR formulary OR trend OR "cost driver" OR "patient satisfaction" OR reimbursement
#16	Poland OR "United Kingdom" OR "UK" OR Germany OR Italy OR Denmark OR "United States" OR "US"
#17	#14 AND #15 AND #16
#18	randomised OR randomized OR "double-blind" OR "cross-over" OR crossover
#19	#17 NOT #18

Table I. Search strategy for PubMed.

Source: Own elaboration.

Collection	Search Strategy for SCOPUS
Copayment	(((TITLE-ABS-KEY-AUTH(coinsurance))OR(TITLE-ABS-KEY-AUTH(copayment))OR(TITLE-ABS-KEY-AUTH(deductible))OR(TITLE-ABS-KEY-AUTH(consumerdirectedhealthplan))OR(TITLE-ABS-KEY-AUTH(healthsavingsaccount))OR(TITLE-ABS-KEY-AUTH(costsharing))OR(TITLE-ABS-KEY-AUTH(referencepricing))))AND(((TITLE-ABS-KEY-AUTH(pharmaceutical*))OR(TITLE-ABS-KEY-AUTH(medicine*))OR(TITLE-ABS-KEY-AUTH(drug*)))AND(((TITLE-ABS-KEY-AUTH(access))OR(TITLE-ABS-KEY-AUTH(quality))OR(TITLE-ABS-KEY-AUTH(equity))OR(TITLE-ABS-KEY-AUTH(efficiency))OR(TITLE-ABS-KEY-AUTH(healthoutcome))OR(TITLE-ABS-KEY-AUTH(effectiveness))OR(TITLE-ABS-KEY-AUTH(utilization))OR(TITLE-ABS-KEY-AUTH(expenditure))OR(TITLE-ABS-KEY-AUTH(spending))OR(TITLE-ABS-KEY-AUTH(payment*)))AND(LIMIT-TO(SUBJAREA,"MEDI")ORLIMIT-TO(SUBJAREA,"HEAL")ORLIMIT-TO(SUBJAREA,"ECON"))AND(LIMIT-TO(LANGUAGE,"English"))
Distribution	(drug* OR medicine* OR generic OR pharmac*) AND (distribution OR deliver* OR delivery OR sale) AND (wholesale* OR intermediating distributors OR chemists OR drugstore OR pharmacy OR Pharmaceutical compan* OR producer* OR manufacturer*) AND ((margin* OR mark-up*) OR (discount* OR bonus* OR rebat* OR subsid* OR fee* OR marketing service*) OR (price* OR net selling OR net purchase OR retail OR wholesale) OR (direct OR indirect) OR (incentives) OR (PBM OR pharmacy benefit management) OR (annual amount of sale OR earnings OR profits OR benefits OR market share) OR (online market) OR (availability OR equity OR access OR accessibility OR affordability) OR (parallel import) OR (law OR regulations) OR (adherence OR compliance) OR (financing AND model* OR system* OR scheme*))

Table II. Search strategy for SCOPUS.

Source: Own elaboration.

list of publications addressing the applicable areas of interests. Papers found to be particularly appropriate were analyzed and the authors of these papers were tracked to include additional relevant papers, if any. Other essential papers known to experts were also included. The manual

search was performed by individuals responsible for the respective area of interest.

The identified papers were added to the bibliography; the most important data were extracted to pre-defined tables and short descriptions were added.

Next, as in the previous step, all information collected so far was assessed from the factual point of view. If any particular area of interest was considered to be covered by insufficient or inadequate data, it was qualified for further research, as was the case in the systematic review.

Methodology of quality assessment

The next step was the quality assessment of the identified publications and adjustment of robustness of extracted data to the quality of source publications.

A bibliography list was compiled from both reviews. Publications included therein represented a broad spectrum of research design. It also included papers without any specific design which nevertheless contained some useful information. The area of research – covering the overall healthcare systems – made the quality assessment particularly difficult as it included descriptions of many types and outcomes of possible and existing interventions which have never been appropriately and comprehensively identified, described and categorized in the literature.

According to expert opinion, we chose to assess the quality of the actual contents of the identified publications (with economic papers prevailing) on the basis of methodology described by West et al. [6]. This tool appeared to be appropriate for the critical appraisal of the contents of all identified literature, including health economics literature data, and all included publications were assessed accordingly.

The critical appraisal of all collected publications was based on three aspects found by West et al. consistency, coherence and strength.

- Consistency – the extent to which diverse approaches, such as different study designs or populations, for studying a relationship or link between a factor and an outcome will yield similar conclusions.
- Coherence – whether the cause-and-effect conclusions conflict with what is known of the reality.
- Strength – the size of estimated effect.

Each of these categories was graded as high, moderate or low.

The above mentioned methodology proved to be insufficient as it did not include any assessment options of design-specific sources of bias, selected outcomes or selected method of obtaining outcomes (such as statistics, etc.). As there is no ready-to-use tool to critically appraise all types of publications, and in order to avoid the bias of inappropriate use of a tool designed to assess quality of one type of research to the other, composite criteria were selected for the quality assessment.

The identified publications were classified into three main categories:

1. Systematic reviews and meta-analyses.
2. Trials and studies which could be described as observational studies in terms of their design, provided they were not in a whole health care system setting.
3. Literature polemics, descriptions of healthcare systems and results of conducted non-systematic literature reviews.

We chose to use a tool created for the assessment of methodological quality of systematic reviews – com-

bined PRISMA and MOOSE checklists developed by Liberati et al. [7] and Stroup et al. [8, 9] for category 1 of the identified publications (systematic reviews and meta-analyses). To make it similar to the other three categories (consistency, coherence and strength described by West et al. [6]) of already performed assessment, we chose three-level evaluation as well, and we reported the results broken down into quality levels: low, medium and high. Classification was made by competent experts and was susceptible to bias as it was subjective because PRISMA and MOOSE checklists do not summarize into a numeric score. For category 2 of the identified publications, the STROBE checklist (Vandenbroucke et al. [10]) (<http://www.strobe-statement.org>) was chosen and the results were also reported as low, medium and high quality. Likewise, the STROBE checklist did not provide any summary score and the classification made by competent experts was therefore subjective.

The quality was not possible to be critically appraised in all identified papers. The methodology of category 3 publications in our categorization list was highly individual and therefore it was not possible to assess its quality.

All categories were assessed by two reviewers independently, who were responsible for each relevant area of interest as the expert's knowledge of literature on a particular topic was an essential component of the assessment. The results of this evaluation were listed into the quality assessment table (Table IV).

The results of systematic and non-systematic review

The final date of performing the review was 28th October 2012, which is considered the cut-off date.

As previously assumed, the identified publications were reviewed and divided to collect separate sets of data relevant to the defined areas of interest. The systematic review produced the total number of 14 723 hits. On screening the titles or abstracts from the databases, 14 489 publications were excluded from the analysis. The remaining 234 abstracts were included into the full-text analysis. Finally, 145 full-text articles were excluded and 89 full-text publications were included in the bibliography collection.

32 full-text publications and articles identified in the non-systematic review were added to the bibliography collection.

To sum up, the two types of reviews identified 89 and 32 full-text publications from systematic and non-systematic reviews, respectively, and the total number of 121 texts was finally included in the analysis [1–5], [11–124]. A complete bibliographic list of full-text publications was prepared. The results of the overall literature review are presented in **Figure 2**.

The results of the literature review broken down into specific areas of interests/collections are listed in **Table III**.

In accordance with the search strategy, out of 14 723 abstracts found in Medline, Embase, Cochrane Library and SCOPUS, the number of included abstracts (listed in brackets) for the relevant collections were as follows: Access and Copayment (196), Health Systems (38).

Collection	Number of included abstracts (Systematic Review)	Number of included full texts (Systematic Review)	Number of included full texts Reference/other sources (Manual search)	Final number of included full texts
Access & Co-payment	196	72	5	77
Health Systems	38	17	27	44
Summary	234	89	32	121

Table III. The results of the review.

Source: Own elaboration.



Figure 2. Results of literature review.

Source: Own elaboration.

Once full texts were reviewed, the number of included articles and publications decreased to: Access and Copayment (72), Health Systems (17).

The non-systematic review revealed a number of relevant publications which the systematic review did not find. Thanks to the non-systematic review the number of added publications was as follows: Access and Copayment (5), Health Systems (27).

Both types of reviews produced the following number of publications: Access and Copayment (77) [1, 3, 5, 11–84], Health Systems (44) [1–4, 85–124].

The results of quality assessment of the identified publications (4-dimensional analysis – consistency, coherence, strength assessment and quality, if appropriate)

The overall number of publications qualified for further analyses was 121; all have been assessed for quality.

All collected publications were assessed in terms of three parameters (consistency, coherence and strength). 25.62% of publications [1, 3, 5, 14, 15, 17, 18, 25, 29, 30, 32–34, 37, 38, 40, 46, 50, 55, 56, 59, 67, 68, 71–73, 75, 77, 78] represented high levels of consistency. 30.58% of publications represented high levels of coherence [1, 3, 5, 14, 15, 17, 18, 21, 23–25, 27, 29, 30, 32, 33, 37, 38, 40, 44, 46, 50, 55, 56, 59, 63, 67, 68, 71, 73, 75, 77, 78], whereas 15.70% of publications revealed high levels of strength [1, 3, 5, 14, 21, 25, 44, 46, 50, 55, 64, 69, 70, 98, 104, 105, 114, 122].

51 of all included publications (42.15%) were classified as meta-analyses, literature reviews and studies and were to be assessed in accordance with the appropriate checklist (PRISMA, MOOSE or STROBE). As a result, 33.33% of publications represented high levels of quality [18, 25, 30, 33, 37, 41, 42, 44, 52, 56, 63, 68, 72, 73, 77, 83, 84]. 47.06% and 19.61% of publications represented medium and low quality levels, respectively. Only 0.83% of publications were graded high in all four parameters (four-dimensional evaluation: consistency, coherence, strength, and quality) [25]. The results of the quality assessment are presented in **Table IV**.

Discussion

Only 0.83% of the identified publications addressing the analyzed areas of drug policy and access management to reimbursed medicinal products in the United Kingdom, Denmark, Germany, Italy and Poland were found to represented high levels of quality in the four-dimensional evaluation. This is the reason why random assortment of scientific literature may involve a high probability of identifying and using publications of poor quality or containing data which do not reflect the reality. It should be underlined that, under scientific circumstances, an accurate and reliable picture of reality can be only produced from data presented in all a variety of different publications instead of a single source of information. The methodology of using two reviewers combined with quality assessment of the identified publications allows to select articles presenting high quality data. In the light of the results presented in this paper, a scientific approach to the literature selection should be recommended whenever possible. Moreover, from the point of view of the public officials, it is important to attempt to improve the publication assortment by relying on widely acknowledged

Collection	Consistency			Coherence			Strength			Quality			Used checklist		No of publications
	L	M	H	L	M	H	L	M	H	L	M	H	A	N/A	
Access and Co-payment	0	47	30	1	40	36	1	63	13	9	16	17	42	35	77
Health Systems	3	40	1	2	41	1	10	28	6	1	8	0	9	35	44
Summary	3	87	31	3	81	37	11	91	19	10	24	17	51	70	121

Legend: L – low, M – medium, H – high, A – applicable (one of the checklists used: PRISMA, MOOSE or STROBE), N/A – not applicable

Table IV. The quality assessment results – summary.
Source: Own elaboration.

rules of data selection and quality assessment. Additionally, it is highly important to spend sufficient amount of time on the review process in order to properly conduct the systematic literature review and to avoid mistakes that could result in a scientific bias.

The assessment of literature review presented in this paper involves specific limitations. It covered papers identified with the use of the adopted strategy instead of data derived from governmental reports. Although it was attempted to cover a broad spectrum of possible areas of interest, we were able to target a slightly different literature than the one used by the authors of such reports. Our own search strategy was used because none of such strategies was revealed in any of the reports in question. It is also possible that the authors of the reports could have been familiar with particular sources of information and deliberately did not search for them while preparing the reports. Therefore, it cannot be ruled out that the actual percentage of high-quality sources and data is different from the one identified in this paper. However, bias is likely to be produced by relying solely on sources known to the authors, with no account taken of their quality, or without updating and screening for new information.

The methodology of quality assessment of economic publications developed by West et al. [6] did not include any assessment of design-specific bias. As there is no tool appropriate to critically appraise all types of publications, we chose to add one more category to the quality assessment of identified publications. After grouping papers according to their design, we chose widely accepted, but not summarizing into a numeric scores checklists (PRISMA, MOOSE and STROBE) for the quality assessment of each group of found publications. The potential limitation of this assessment was that outcome was subjective and susceptible to bias.

As we mentioned before, the quality was not possible to be critically appraised in all identified papers. There also have been papers without any specific design, but containing some information useful for our objectives and considered important as being unique source of specific detailed information. We did not assess at all the quality of their design and that was the next possible limitation of our work.

Conclusions

A large number of publications strictly addressing the defined areas of interest were identified and included in this analysis of availability and quality of data. 42.15% of them, to a large part consisting of studies, meta-analyses and reviews, were identified as relevant in terms of quality assessment. 33.33%, 47.06% and 19.61% of the identified publications were classified as high-, medium- and low-quality publications, respectively. Moreover, data on some areas of interest were found to be scarce or missing. There were no comparable analyses found and no relevant reliable data available. To improve the quality and reliability of information available to decision makers, multiple sources should be used, identified by means of the broadly accepted methodology of searching for papers in all available databases and assessing the quality of the identified materials by the best and the most accepted methods, at least to the extent possible.

Conflict of interests

None was declared.

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