**Supplementary Material 2:**

**Re-ADAPT framework for the assessment of medicine price data sources (full version)**

| **Criterion** | **Recommendation** | **Rationale** | **Checklist** |
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| *Overarching principle*  The objective of the study (research question), or any other purpose of the medicine price data collection (e.g. price data for use in external price referencing), is decisive in the assessment of the data sources, in general and with regard to the assessment criteria. | | | |
| *Mandatory criteria* | | | |
| **Re**liability and sustaina­bility | The use of data from established and well-known sources is strongly recommended. Researchers are urged to contact managers of unknown data sources in advance to explore reliability. | Summary: Researchers should ensure that data are provided from the chosen price data source as stipulated by the data source providers, in the defined format, at the delivery time as agreed and at the negotiated / agreed costs.  Key considerations:  Reliability of a data source is considered a major prerequisite for selection. It would indeed be a most unpleasant surprise if during the data collection (or a follow-up check) the source were no longer accessible because the website has meanwhile been shut down, for instance. Equally annoying would be the non-arrival of ordered price data, especially if payment had already been made, and, even worse, no contact of the data source could be reached. Thus, researchers should ensure that they do not fall for a fake provider. Another cause for the discontinuation of a source could be that a price database was established for research purposes but due to lack of resources it is no longer maintained and/or updated after the end of the project. Thus, sustainability of the data source should also be checked.  Another aspect of reliability concerns the appropriateness and soundness of the data. In this respect, more information about the data source, such as their data collection, validation and further quality assurance aspects, provide further guidance. | How to proceed:  Researchers are urged to identify the managers of the data source before they immerge into data collection. A minimum standard is the publication of full contact details of the owner or manager of the source. Data provided by an official body (e.g. a public authority that maintains a database) or of a well-known private provider should be given preference. It can also be helpful to address peers and learn about their experience with different price data sources and providers. Before collecting data from an unknown source, researchers are advised reaching out for the provider of the data, ideally in writing as well as through a telephone call. This is especially key for larger-scale projects. |
| **Re**liability and sustaina­bility *(continued)* |  |  | Checklist questions:   * Who owns / manages the data source? * Are contact details indicated? Were requests answered in due time? * Is it a new data source, or has it been established for a longer period of time? * Have papers been published that used data from that source? * Have other researchers worked with data of the identified source? What were their experiences? |
| **A**ccessibility | It is advised to explore possible accessibility barriers (e.g. costs, registration, non-eligibility). The decision should be taken by balancing identified benefits and limitations of protected and/or expensive data sources and medicine price services. | Summary: Accessibility of a data source may be limited by different restrictions. In principle, there are three options of how data can be accessed:  First, price data can be freely accessible, and, as such, they require neither registration nor a password nor do they entail any costs. Examples: The Australian Department of Health provides a web-based searchable database with price information of medicines subsidized by the Australian Pharmaceuticals Benefits Scheme (<http://www.pbs.gov.au/pbs/home>). The Brazilian Medicines Agency offers price lists for download (<http://portal.anvisa.gov.br/listas-de-precos>).  Second, accessibility can be limited and will only be granted after the data providers have checked the user’s eligibility status. Under this option, access to a price database can be linked to user charges. Examples: The Management Sciences for Health (MSH) guide (<http://mshpriceguide.org/en/home/>) that publishes international reference prices for medicines requires registration for customized queries (the guide itself is freely accessible). The Western Pacific Platform for Procurement Price (PIEMEDS), a password-protected platform, also manages two accessibility levels: Upon registration, anyone can access price information of few medicines of the involved countries. Only country representatives (that also provided data for their countries) are allowed to access medicine price data of all included medicines, such as new high-cost medicines (<https://piemeds.com/> ).  Third, requested data can be provided through a service, usually against payment: this means that access to the primary data source is not possible; instead, data in a defined scope (e.g. all reimbursable medicines, hospital medicines) and presentation (e.g. price data per pack) will be supplied. Examples: A well-known example is the commercial provider IQVIA (previously IMS Health; <https://www.iqvia.com/> ). In the non-profit area, the Austrian Public Health Institute offers requested price data for medicines, against charge for coverage of working time, through their Pharma Price Information (PPI) service (<https://goeg.at/Pharma_Price_Information> ).  Key considerations:  All three approaches have benefits and limitations.  The first option offers the advantage that researchers can immediately validate the appropriateness of the source and, in case of a positive assessment, collect the data without further delay. Also, no funding needs to be raised. Despite of these benefits at first glance, freely accessible data sources should still be critically assessed with a view of their compliance with other criteria, in particular reliability. | How to proceed:  Researchers should investigate whether, or not, and which limitations are linked to data sources. Even if a freely accessible data source was identified, researchers are encouraged to still search for alternative data sources that might be more appropriate for the research question. If a data source with access restrictions (in particular costs) was identified, researchers are advised to ask for free sample data before placing a large order.  Checklist questions:   * Is data freely accessible? Do users have to register? * Is the source password-protected? For how long are users granted access to the protected source (at one point in time or for a longer period)? * Who is eligible for accessing the database? Do I meet the eligibility criteria? * Is it a price service that offers customized findings? How much time does the delivery of ordered data take? * How much do the medicine price data cost? Does payment for data cover a full package, or may further costs for additional follow-up queries be charged? Are discounts granted to researchers? |
| **A**ccessibility (*continued)* |  | The second option, and also the third option, are generally connected to some transaction costs in terms of time and money. Time to discuss the request with the managers of the source likely needs to be invested and may result in the decision that data from a short-listed source will eventually not be used. Researchers may have to wait for some time until the request will be successfully handled (e.g. access being granted to a database, delivery of data from a service). Costs can also be substantial. Researchers are advised exploring possible discounts that might be offered if data are used for research purposes, or by research institutions.  A medicine price service, the third option, offers the advantage that in return for investments (costs and negotiation time), time resources are saved since primary price data collection is delegated to others. This is particularly a benefit if large amounts of data are needed. When researchers decide to order data from a medicine price service, they may also request receiving additional information required for the analysis (e.g. prescription status, patent status, designation as an orphan medicinal product according to European legislation or as a hospital medicine according to national legislation, volume data).  Searching for the most appropriate data sources, researchers might explore hybrid solutions. For instance, accessibility of a price database can be limited to its members who established it (e.g. public authorities, such as the above-mentioned PIEMEDS database), but researchers may still be granted limited access or may receive a defined data set. |  |
| **D**ate | It is discouraged using data from a source whose date is not disclosed. | Summary: It is crucial that researchers know the date the price data refer to. Otherwise there is the risk that they work with out-dated information or they compare data of different points of time. If there is lack of knowledge about the date, price data cannot be computed or standardised correctly (e.g. inflation-adjustment for time series analyses, application of the exchange rates of the respective dates).  Key considerations:  Data that are provided for a period of time should be presented in the same way throughout the observation period. This concerns all possible aspects of characteristics of price data (e.g. price types, formats such as dosage aggregates of pack, units, DDD, inclusion of taxes, etc.). Elsewise, changes (e.g. breaks in the methodology) should be clearly indicated to allow an informed decision of whether, or not, these changes are acceptable and could be ‘repaired’ (e.g. if missing price types such as ex-factory prices can be computed thanks to statutory distribution mark-up regulation, see below the criterion ‘price type’) or if researchers should rather identify another data source. | How to proceed:  Researchers that are interested in doing time series analyses or who require price data of a specific date are advised to check whether, or not, the data source continues offering historical data. It was observed that several databases updated on a daily basis or at other regular intervals no longer offer data of time periods before the update.  Checklist questions:   * Which dates do the price data refer to? * How frequently is the data source updated? * Does the data source also provide historic data, and at which intervals? Are historic price data presented in the same way over the years? |
| Geographic scope (**a**rea) | It is advised selecting data sources that provide representative price data for the defined geographic area (e.g. a country). | Summary: A geographic area can relate to a country, or countries, as well as to smaller units of a country (e.g. region, municipality, city). Depending on the existence of the pharmaceutical pricing policy framework and its characteristics, prices in a defined geographic area may differ for all or some price types.  Key considerations:  Different pharmacies, dispensaries and retailers of medicines within a country or region may dispense or sell the same medicine at different prices. Intra-country price variation has particularly been observed in settings without price regulation. Price differences may relate to some but not all price types: for instance, ex-factory prices might be uniform throughout a country, but the final consumer prices of some (non-price regulated) pharmaceuticals, such as non-prescription or non-reimbursed medicines, may differ between pharmacies. In the case of reimbursement prices, differences may exist for different payers or for different insured, in case of different health care packages. | How to proceed:  Researchers are advised to explore if legislation in the countries of the study allows for price differences of the same medicine and, should this be the case, if price variation is, at least anecdotally, known from practice. If a data source cannot ensure representative coverage of different dispensaries, researchers are discouraged from using its data. Eventually, this limitation may incentivise them to explore a primary data collection through on-site surveys.  Use of data from different sources (e.g. in cross-country price comparison that is based on national price databases) is, in principle, a feasible methodological choice if attention is paid to ensure comparability of the price data.  Checklist questions:   * Does the data source offer information that is valid for the whole country (or any other defined geographic area)? * If this is not the case: does it specify gaps? |
| Scope of **p**harma-ceuticals | It is advised checking the coverage of the medicines included in the data source. | Summary: A major methodological choice of a price study is the selection of medicines and/or groups of medicines analysed. Since data sources are frequently restricted to certain market segments, possible candidate sources should be checked as to whether they contain data of the selected medicines. Some data sources do not provide information about the scope of medicines they cover.  Key considerations:  Price data sources have been established for different purposes and, as a result, include a different range of data. It can be expected that a procurement price database is limited to medicines procured through tenders, and that prices retrieved from data sources managed by reimbursement agencies tend to be focused on publicly subsidised pharmaceuticals. Sources of price information that are based on sales data likely include solely medicines that represent sales whereas administrative data sources might provide price information for medicines that received a price even if eventually the medicines have not been marketed. Data source providers frequently have ownership of, or access to, price data of parts of the market. For instance, data sources of social insurance institutions that are responsible for the outpatient sector do usually not provide information about medicines exclusively used in hospitals. Price data of some medicine groups may not be included in a data source because no uniform price data within a geographic area (e.g. a country), or no price data at all, are available. Even in high-income countries, missing price information has been observed, particularly for hospital medicines (different procurement prices between hospitals or hospital groups) as well as for non-funded and/or non-prescription medicines. Non-availability of price data of the latter results from a situation that non-funded and non-prescription medicines are not price–regulated in several countries, and their prices are not published in official price lists.  To the authors’ experience, many price data sources do not inform about their coverage. However, missing information of coverage does not imply that all medicines are included. | How to proceed:  Researchers are urged to carefully review if the medicines they aim to include in their research are covered in the selected data source. If the data source is publicly available, it is recommended searching in advance, during the assessment of the source, for the medicines needed for the study, at least on a sample basis. In case of accessibility of the data source against costs, it is advised asking the managers of the data source about the medicines included. A demo sample version, if made accessible, could be analysed with a view of exploring its usefulness for the planned study. The investigation of a sample also allows getting a better understanding of the set-up of the source and its presentation of the data.  Checklist questions:   * Does the data source offer price information for all medicines, or at least for the required groups of medicines? * Does the data source specify which medicines (e.g. non-prescription, non-funded, hospital-only medicines, those not marketed) are not included? * Does the source provide price information for all medicines listed, or are some pharmaceuticals indicated without a price? * Is it explained why some price information has not been included in the data source? |
| Price **t**ypes and further specifi­cations of price data | It is advised checking whether, or not, the source provides price information for the price types selected for the research. The choice of the price types should not depend on the data source but it should be aligned to the purpose of the study. | Summary: Under the label of ‘medicine price data source’, different price data can be offered, and some of them are not price data but other data (‘price proxies’). If they are price data, they can refer to different price types, and they can be presented in different formats of dosage aggregation.  Key considerations:  Some data sources pretend to offer medicine price data but in fact they offer other economic data, such as expenditure data. For a price study, expenditure or sales data are, in principle, not correct; these data are useful for other research purposes. In a few exceptional cases, using expenditure and volume data to develop a ‘price proxy’ can be acceptable depending on the study objective. In most cases, however, original price data are required.  Key characteristics to define price data are price types and the formats of how data are presented.  Common price types for outpatient medicines in price–regulated countries are the ex-factory price (manufacturer price), the pharmacy purchasing price (wholesaler price) and the (pharmacy) retail price (consumer price) including or excluding taxes (typically the value-added tax). Price studies in the inpatient sector likely consider procurement prices that correspond to ex-factory prices, since supply chain add-ons usually do not come into play for hospitals that tend to dispense medicines solely to inpatients. Besides list prices, discounted prices may exist at the ex-factory, wholesale and retail price levels due to price reductions granted by suppliers to the purchasers. The extent of discounts is often confidential, particularly if they are the result of negotiations between a payer and a pharmaceutical company, but in some cases, such as for mandatory discounts provided for in legislation, discounts are known.  The medicine price study can be done for different price types depending on the study objective. Even if price data for the selected price type, or price types, to be analysed in the study are not available in the assessed source, data can be calculated from price data in some cases. For instance, the pharmacy retail price can be derived from the ex-factory price indicated in the data source by applying statutory wholesale and pharmacy mark-ups. However, this is only possible if the remuneration of supply chain actors is regulated, and in a way that it depends on the medicine price (e.g. as mark-ups or margins, and not a price-disconnected dispensing fee or other fee-for-service remuneration). | How to proceed:  Researchers have to define in advance which price data they require (in particular with regard to the price type but also for other methodological choices discussed in the section of different assessment criteria). In the methodology development process, researchers should also decide if and which price proxies could be acceptable if no price data were accessible. With line with the definition of price data, researchers should then check whether the source provides the data for the required price type(s) and in the requested format. If not, it shall be checked whether it is possible to derive the required price type(s) and format through further calculation of data retrieved from the data source.  Checklist questions:   * Does the source provide price, expenditure or cost data? * Are price data offered for single presentations (i.e. medicines in a defined pharmaceutical form, dosage and pack size)? * At which price type, or types, does the source offer price information? Are the indicated price types those that were selected for the analysis? * Is the format of how data are presented clear? Can price information be standardised to allow the use of data from different sources, in line with the study objective? |
| Price **t**ypes and further specifi­cations of price data *(continued)* |  | Cross-country comparisons must be conducted at the level of the same price type. Therefore, it has to be explored in advance whether the data sources of different countries offer the selected price type or, alternatively, allow a determination of the required price types as described above.  The format of how price data are presented (e.g. per pack, per Defined Daily Dose (DDD), per ‘standard unit’, per treatment course) must be clear. Though variation in the data presentation of different sources constitutes a methodological challenge, this can be handled by means of appropriate standardisation under the condition that information required for doing the standardisation is accessible.  Finally, it is also recommended checking if price data are consistently provided for all medicines listed in the source. This advice is based on the experience that some databases list all medicines that received a marketing authorisation, but they provide price information for only some of them. |  |
| *Secondary criteria* | | | |
| Easy handling | While the ‘comfort function’ is less decisive for the selection of a data source than mandatory criteria, it could also be considered. Complex and time-intensive data retrieval should be accounted for in the planning process. | Summary: Data can be provided in different technical solutions that can range from paper lists to electronic query standards. The way of how the information is presented in a source may considerably impact the time resources required for collection and follow-up manipulation of the data.  Key considerations:  Data provision through a website does not automatically imply easy handling. For instance, the collection might be time-intensive if each price data point has to be retrieved separately because no download function is provided.  The features of the search function are another aspect to consider. Some sources allow searching by International Non-Proprietary Name (INN) or by ATC code, whereas others require a search by trade name. If the latter is the case, additional time is needed to first identify the appropriate trade names through other searches (e.g. in a register that contains all authorised medicines) since trade names can differ across countries. If for a generic medicine price study the lowest-priced generic is aimed to be identified, a source that allows identifying, selecting and ranking available generic versions is preferred to manual data retrieval and manipulation. Similarly, the lack of filters for inclusion, or exclusion of, specific groups (non-reimbursed, non-prescription or non-marketed medicines) likely increases the working time to collect and process the data. | How to proceed:  Researchers should test the retrieval of the data (in freely accessible data sources or in a demo version) and, if data collection turns out to be cumbersome, plan sufficient time resources. Researchers can also address the data source providers and ask whether data could be provided in a more easy to handle solution (e.g. set of raw data that is fed in a web database).  Checklist questions:   * Is the source electronically available? * Can the data be easily retrieved and transferred into a format required for further analyses? * Does the source allow for the collection of several data points at one time, or do you have to retrieve each single data point separately? * How are data stored in the source, and how are stored data made accessible to the data collectors? |
| Additional information | If further (not price–related) information about the studied medicines is required, its provision in a data source might be beneficial. | Summary: For a price study, further information about the medicines (e.g. their reimbursement and/or prescription status, dispensing rules, prescribing prerequisites) can be helpful and is, in some cases, essential.  Key considerations:  Research might be focused on specific market segments such as the reimbursement, outpatient or prescription-only medicines sectors, and features that help identify medicines of defined sectors is appreciated. Further needed data might be volume data if price indices are planned, for instance. If such data are required for research, their provision in the identified data source is an appreciated supporting service. | How to proceed:  Researchers should identify in their study protocol possible additional data that they may need.  Checklist questions:   * Which additional information is provided by the source? * Are there pieces of additional information essential for the research question? |