Evaluation of the relevance of Embase for searching for drug studies[1]

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This report was prepared without the involvement of external experts.

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Executive summary

In the context of the general commission awarded to the Institute for Quality and Efficiency in Health Care (IQWiG), the topic of evaluating the relevance of the Embase bibliographic database for searching for drug studies was addressed.

Research question

The objectives of this evaluation were:

- to analyse the availability of drug studies in Embase that are not included in MEDLINE or the Cochrane Central Register of Controlled Trials (CENTRAL) and
- to evaluate the necessity of searching for drug studies in Embase in the context of IQWiG's comprehensive information retrieval process.

Methods

Studies from dossiers submitted by drug manufacturers (Data pool 1: dossiers) were considered. Studies from completed final reports and rapid reports on past drug assessments were also considered (Data pool 2: IQWiG reports/rapid reports on drug assessments).

An analysis was performed based on the information available for the MEDLINE, CENTRAL, and Embase databases. Journal articles that were only indexed in Embase were examined in more detail, including an evaluation of the importance of the underlying studies for the respective benefit assessment.

Results

Data pool 1: Dossiers

The analysis included 723 dossiers, comprising 3028 journal articles on 2126 studies.

When searching bibliographic databases, 4 journal articles were identified exclusively via Embase. Only 1 of these 4 studies was classified as relevant in the corresponding dossier assessment (A20-36). In addition, further publications or documents on results (e.g., study report) were available for all 4 studies.

Overall evaluation of searching Embase for drug studies in the context of the early benefit assessment of drugs

In the context of the early benefit assessment of drugs, searching Embase in addition to MEDLINE and CENTRAL is considered unnecessary, as no additional information relevant to the assessment is expected to be found. Omitting this search is unlikely to have any

consequences relevant to decision-making. A separate search in Embase does not appear to offer any relevant added value.

Data pool 2: IQWiG reports/rapid reports on drug assessments

The analysis included 34 IQWiG reports/rapid reports on drug assessments, which comprised 1560 journal articles on 736 studies. When searching bibliographic databases, 15 journal articles were identified exclusively via Embase.

Overall evaluation of searching Embase for drug studies in the context of IQWiG reports/rapid reports

In the context of IQWiG reports/rapid reports, searching Embase in addition to MEDLINE and CENTRAL is considered unnecessary, as no additional information relevant to the assessment is expected to be found. Omitting this search is unlikely to have any consequences relevant to decision-making. A separate search in Embase does not appear to offer any relevant added value. In the present analysis, only one journal article identified exclusively via Embase out of a total of 587 studies was found to have an influence on the conclusion of the report. This isolated case is insufficient to justify a regular search in Embase.

Conclusion

In the context of comprehensive information retrieval for IQWiG's benefit assessments of drugs, searching Embase in addition to MEDLINE and CENTRAL is considered unnecessary. Omitting this search is unlikely to have any consequences relevant to decision-making. A separate search in Embase does not appear to offer any relevant added value. This is particularly the case for studies initiated after 2007, when a legal requirement to register clinical trials was introduced in the United States

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List of abbreviations

Abbreviation	Meaning
CENTRAL	Cochrane Central Register of Controlled Trials
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MECIR	Methodological Expectations of Cochrane Intervention Reviews
RCT	randomized controlled trial

1 Background

Information retrieval for the preparation of systematic reviews of interventions should always include a search of bibliographic databases, in addition to other sources. There has been a long-standing debate in the literature about how many and which databases are necessary to identify all relevant data for the assessment [1].

Previous research shows that searching a limited number of databases is sufficient to comprehensively identify studies on medical interventions [2-5]. This applies not only to searches for randomized controlled trials (RCTs) [3], but also to non-randomized studies [6]. The assumption that including many databases leads to better results is often not true [7].

MEDLINE[2] plays a central role in deciding which databases to include in the search. Between 84 and 92% of the RCTs included in Cochrane Reviews are in PubMed [3,4,8]. In addition to its extensive coverage, a further advantage of MEDLINE is the Medical Subject Headings (MeSH) system [9], which is a comprehensive controlled vocabulary used to index journal articles. Furthermore, a large number of search filters (e.g., for identifying RCTs [10] or systematic reviews [11]) have been created for MEDLINE over the years. This greatly simplifies searching in this database and enables tailored and precise searches.

The Methodological Expectations of Cochrane Intervention Reviews (MECIR) [12] require a search in CENTRAL, MEDLINE (e.g., via PubMed), and Embase (if Embase is available to either the Cochrane Review Group or the author of the review). Since Embase is not listed as mandatory in MECIR, the question arises as to whether this database can be dispensed with entirely for certain research questions. The analysis by Metzdendorf et al. 2019 [6] shows, for example, an indexing rate in PubMed of 94% for drug studies.

Despite its comprehensive coverage of biomedical literature, Embase has some limitations that should be taken into account when conducting systematic reviews. A key criticism is the high licensing cost, which can be a major hurdle, especially for smaller research institutions. In addition, sensitive search strategies in Embase often lead to imprecise results, significantly increasing the number of irrelevant hits. Closely related to this are less well-developed and validated filters for different study types or specific populations. This also makes it difficult to narrow down search results precisely. In view of the existing limitations, omitting Embase seems to be a reasonable measure to increase efficiency and save resources.

[2] In the literature, PubMed and MEDLINE are often used synonymously. Since MEDLINE is the central component of PubMed, MEDLINE will be used consistently in the following, unless PubMed is specifically addressed in a journal article.

2 Research question

The objectives of this evaluation were:

- to analyse the availability of drug studies in Embase that are not included in MEDLINE or the Cochrane Central Register of Controlled Trials (CENTRAL) and
- to evaluate the necessity of searching for drug studies in Embase in the context of IQWiG's comprehensive information retrieval process.

3 Course of the project

A working paper was prepared on the basis of an internal project outline. This report was submitted to the Federal Joint Committee (G-BA) and published on the IQWiG website 4 weeks later.

4 Methods

The work was carried out in several steps. Based on the analyses of Data pool 1 (dossiers) and Data pool 2 (IQWiG reports/rapid reports on drug assessments), the relevance of Embase for comprehensive information retrieval for drugs is assessed.

4.1 Data pool 1: Dossiers

4.1.1 Information retrieval

The data pool was created from the dossiers assessed by IQWiG for benefit assessments pursuant to §35a of the German Social Code, Book V (SGB V). From the studies listed in the dossier, those included in the benefit assessment by the drug manufacturer were used, together with the associated publications.

Data routinely collected by IQWiG's Information Management Department were used. Accompanying the dossier assessments, the studies listed in the dossiers were recorded in an internal Access database. Information on the studies was taken from the respective study pool tables in Module 4 of the dossier (e.g., Table 4-5 of the dossier template [13]). In accordance with the requirements for dossiers [13], this includes journal articles on the studies submitted, provided that these were identified through information retrieval conducted by the drug manufacturers. For CENTRAL and Embase, only those journal articles not indexed in MEDLINE were included in the Access database. Studies listed in the "Further investigations" section were only included in the Access database if the number was < 10.

Studies from dossiers covering the period 2011 to 2024 and included in the internal Access database by 30 July 2024 were taken into account. No duplicate check was performed at the study and journal level.

Assessments and underlying dossiers pursuant to §35a (1), Sentence 11, SGB V were not taken into account. These are assessments of orphan drugs that are approved for the treatment of rare diseases. These were only taken into account if the sales threshold was exceeded; otherwise, IQWiG does not conduct further assessments.

4.1.2 Evaluation of information

In order to assess the quality of data collection in previous years and thus be able to classify the results of the analyses, the study-related data (completeness of the studies to be considered and information on publications) from the internal Access database were compared with the information in 20 dossiers in accordance with the approach in project GA23-03 [14]. The same dossiers as in GA23-03 were screened again. The dossiers were selected at random, but care was taken to ensure that at least one dossier from each year was included.

In addition, it was checked whether dossier assessments contained references to other potentially relevant studies that were not included in the study pools of the underlying dossiers. For this reason, all dossier assessments commissioned from 2020 onwards and published by 31 May 2023, including associated addenda, were also screened. Where such studies were found, they were documented and considered in the analysis.

Several steps were taken to process the data from bibliographic databases:

- Standardization of accession numbers in Embase
- Deletion of Embase entries if a MEDLINE entry for the same citation existed in the Access database
- Deletion of entries from other sources (e.g., from EU-CTR or Web of Science)
- Deletion of conference abstracts and errata

4.1.3 Synthesis and analysis of information

Journal articles were analysed at the publication and study level:

- Determination of the proportion of studies with assigned journal articles

Publications indexed only in Embase were examined in greater detail. First, it was checked whether they were indexed in MEDLINE or CENTRAL at the time of the search, but the information in the dossier was incomplete in this regard. To this end, a simple search was conducted in MEDLINE and CENTRAL. In addition, it was checked whether the study could be identified via other sources of information (study registries, manufacturer inquiries).

Finally, an overall evaluation was made as to whether an additional search in Embase would provide relevant added value in the context of comprehensive information retrieval for dossiers.

No relevant added value was determined if:

1) the publication language was not English or German [15,16],
2) further publications or documents on results relating to the study (e.g., study report) were available,
3) the underlying study was formally included but not considered for the benefit assessment,
4) the omission of the publication in question had no impact on the overall conclusion of the dossier assessment (in terms of the probability and extent of any added benefit).

The criteria were applied hierarchically. The analysis was performed in Excel.

4.2 Data pool 2: IQWiG reports/rapid reports on drug assessments

4.2.1 Information retrieval

The data pool consisted of completed final reports or preliminary reports as well as rapid reports on drug assessments. The included studies with associated publications were taken from these. The study pool was based on comprehensive information retrieval by IQWiG.

The information on the individual studies was taken from the respective study pool tables and from the tables on the included studies without reported results. This includes, among other things, the accession numbers of the journal articles from the bibliographic databases MEDLINE, Embase and CENTRAL, as well as other documents identified in the course of the respective information retrieval process. For Embase, only those journal articles not indexed in MEDLINE or CENTRAL were considered. No duplicate check was performed at the study and publication level.

4.2.2 Evaluation of information

Data collection was performed by one person and quality assured by a second person.

4.2.3 Synthesis and analysis of information

The retrieved journal articles were analysed at the publication and study level:

- Determination of the proportion of studies with assigned journal articles

Journal articles only indexed in Embase were examined in more detail. Beforehand, it was checked whether they were indexed in MEDLINE or CENTRAL at the time of the search. In addition, it was checked whether the study could be identified via other sources of information (study registries, manufacturer inquiries).

Finally, an overall evaluation was made as to whether an additional search in Embase would provide relevant added value in the context of comprehensive information retrieval for benefit assessments pursuant to §139a SGB V.

No relevant added value was determined if:

1) the publication language was not English or German,
2) further publications or documents on results relating to the study (e.g., study report) were available,
3) the underlying study was not considered for the benefit assessment,

4) the omission of the study publication in question had no impact on the conclusion of the report/rapid report for any outcome considered in terms of the certainty of the results or the conclusion on (added) benefit (yes or no).

The criteria were applied hierarchically. The analysis was performed in Excel.

5 Results

5.1 Data pool 1: Dossiers

5.1.1 Results of information retrieval and evaluation

Dossiers included in the internal Access database by 30 July 2024, as well as dossier assessments commissioned from 2020 onwards and published by 31 May 2023, including associated addenda, were taken into account. These included 11 studies that were additionally identified through the supplementary screening of dossier assessments and associated addenda and were not listed in the corresponding dossier in the study pool tables. No reference to an additional Embase journal article entry was found for any study identified through the supplementary screening of dossier assessments and associated addenda.

In order to assess the quality of data collection in previous years, the analysis from project GA23-03 was reviewed. As with GA23-03, the data pool was deemed to be of good quality and in line with the requirements.

5.1.2 Results of information synthesis and analysis

The analysis included 723 dossiers, comprising 3028 journal articles on 2126 studies. Of these, 3014 journal articles were indexed in MEDLINE (99.5%) (see Table 1). Only one journal article (ARGON study) was not indexed in MEDLINE, CENTRAL or Embase at the time of the drug manufacturer's search. The manufacturer states that it identified this article through a manual search [17].

A description of the 4 journal articles only indexed in Embase can be found in Table 6, Appendix A. None of the 4 journal articles showed any added value, as further publications or documents on results of the study (e.g., results report) were identified.

Table 1: Data pool 1 - Drug studies in bibliographic databases at the level of journal articles

Indexing in:	Number of journal articles	Proportion of all journal articles
MEDLINE	3014	99.5%
MEDLINE + CENTRAL[a]	3023	99.8%
MEDLINE + CENTRAL + Embase[b]	3027	99.9%
MEDLINE + CENTRAL + Embase + manual search[c]	3028	100%

a. For CENTRAL, citations were only considered if they were not indexed in MEDLINE.
b. For Embase, citations were only considered if they were not indexed in MEDLINE or CENTRAL.
c. For manual searches, citations were only considered if they were not indexed in MEDLINE, CENTRAL or Embase.

In addition, Table 2 shows the analysis at the study level. Of the 2126 studies in dossier assessments, 1711 had a corresponding journal article, while the remaining 414 studies did not. For 1711 of the studies with journal articles, at least one MEDLINE citation was available for 1708 (99.8%). For 2 further studies, 1 CENTRAL citation was available; no other study was indexed exclusively in Embase.

Table 2: Data pool 1 - Drug studies in bibliographic databases at the study level

Indexing in:	Number of studies	Proportion of all studies (N = 2126)	Proportion of studies with journal articles
MEDLINE	1708	80.3%	99.8%
MEDLINE + CENTRAL[a]	1710	80.4%	99.9%
MEDLINE + CENTRAL + Embase[b]	1710	80.4%	99.9%
MEDLINE + CENTRAL + Embase + manual search[c]	1711	80.5%	100%

a. For CENTRAL, citations were only considered if they were not indexed in MEDLINE.
b. For Embase, citations were only considered if they were not indexed in MEDLINE or CENTRAL.
c. For manual searches, citations were only considered if they were not indexed in MEDLINE, CENTRAL or Embase.

Overall evaluation of searching Embase for drug studies in the context of the early benefit assessment of drugs

In the context of the early benefit assessment of drugs, searching Embase in addition to MEDLINE and CENTRAL and other sources of information (study registries and manufacturer documents) is considered unnecessary, as no additional information relevant to the assessment is expected to be found. Omitting this search is unlikely to have any consequences relevant to decision-making. A separate search in Embase does not appear to offer any relevant added value.

5.2 Data pool 2: IQWiG reports/rapid reports on drug assessments

5.2.1 Results of information retrieval and evaluation

A total of 35 IQWiG reports/rapid reports on drug assessments that were included in the internal Access database by 1 November 2023 were considered. In the further evaluation, one IQWiG report (A04-02) was not taken into account because the commission was awarded on the basis of a previously known study and the information retrieval did not reveal any further studies.

5.2.2 Results of information synthesis and analysis

A total of 1560 journal articles on 736 studies in 34 IQWiG reports/rapid reports were included in the analysis. Of these, 1521 journal articles were indexed in MEDLINE (97.5%) (see Table 3).

In addition, 18 citations from CENTRAL, 15 from Embase, and 5 from other databases not indexed in MEDLINE were included.

A description of the 15 journal articles indexed only in Embase can be found in Table 7. With the exception of one, none of the journal articles provided any added value because:

- 2 journal articles were not published in English or German
- for 6 journal articles, additional publications or documents on results (e.g., results report) were identified for the study
- 2 studies were not considered for the benefit assessment
- for 4 journal articles, the omission of the article in question had no impact on the conclusion of the report/rapid report for any outcome considered in terms of the certainty of the results or the conclusion on (added) benefit (yes or no)

One exception is the journal article McPartlin 1998 [18] from report A05-20A (2010) [19]. The results of this study were included in several meta-analyses for a direct comparison of the antidepressant venlafaxine with selective serotonin reuptake inhibitors (SSRIs) as a drug class and with paroxetine as a single drug from the SSRI class. In the overall evaluation, taking into account McPartlin 1998, an added benefit of venlafaxine was shown in comparison with the SSRI drug class (at the level of individual drugs for fluoxetine) for the outcome of response. However, disadvantages were found in individual higher-level adverse event outcomes. If this study publication had not been considered, an added benefit of venlafaxine over the individual SSRI paroxetine would also have been found for the outcomes of response and total score on the depression scales (measured using the Hamilton Depression Scale [HAMD]). The advantages and disadvantages of venlafaxine already identified would remain unaffected. Thus, the conclusion would be expanded to include further advantages of venlafaxine compared with another SSRI and would not be significantly changed in the overall evaluation.

Table 3: Data pool 2 - Drug studies in bibliographic databases at the level of journal articles

Indexing in:	**Number of journal articles**	**Proportion of all journal articles**
MEDLINE	1521	97.5%
MEDLINE + CENTRAL[a]	1539	98.7%
MEDLINE + CENTRAL + Embase[b]	1555[d]	99.7%
MEDLINE + CENTRAL + Embase + other databases[c]	1560	100%

a. For CENTRAL, citations were only considered if they were not indexed in MEDLINE.
b. For Embase, citations were only considered if they were not indexed in MEDLINE or CENTRAL.
c. For other databases, citations were only considered if they were not indexed in MEDLINE or CENTRAL
d. Among the 16 journal articles, there is one duplicate; see Table 7.

In addition, Table 4 shows the analysis at the study level. Of the 736 studies, 587 had a corresponding journal article, while the remaining 149 did not. Of the 587 studies with journal articles, 563 (95.7%) had at least one MEDLINE citation. A further 11 studies had 1 CENTRAL citation and the remaining 8 studies had at least 1 Embase citation.

Table 4: Data pool 2 - Drug studies in bibliographic databases

Indexing in:	Number of studies	Proportion of all studies (N = 736)	Proportion of studies with journal articles
MEDLINE	563	76.5%	95.9%
MEDLINE + CENTRAL[a]	574	78%	97.8%
MEDLINE + CENTRAL + Embase[b]	582	79.1%	99%
MEDLINE + CENTRAL + Embase + other databases[c]	587	79.8%	100%

a. For CENTRAL, citations were only considered if they were not indexed in MEDLINE.
b. For Embase, citations were only considered if they were not indexed in MEDLINE or CENTRAL.
c. For other databases, citations were only considered if they were not indexed in MEDLINE or CENTRAL.

Overall evaluation of searching Embase for drug studies in the context of comprehensive information retrieval

In the context of IQWiG reports and rapid reports on drugs, searching Embase in addition to MEDLINE and CENTRAL and other sources of information (study registries and manufacturer documents) is considered unnecessary, as no additional information relevant to the assessment is expected to be found.

In the present analysis, only one journal article identified exclusively via Embase out of a total of 587 studies was found to have an influence on the conclusion of the report. This isolated case is insufficient to justify a regular search in Embase.

5.3 Summary of the search for drug studies in bibliographic databases

The analyses show that the majority of journal articles on drug studies are indexed in MEDLINE and CENTRAL (see Table 5).

Table 5: Summary of the search for drug studies in bibliographic databases

	Number of IQWiG reports/rapid reports analysed (studies[a])	Number of journal articles	Number of journal articles indexed exclusively in Embase	Added value of searching Embase
Data pool 1: Dossiers	723 (1711)	3028	4 (0.1%)	No
Data pool 2: IQWiG reports/rapid reports on drug assessments	34 (587)	1560	15 (1%)	1 study
Total	**757 (2298)**	**4588**	**19 (0.4%)**	

a. Study with at least 1 journal article on the study.

6 Discussion

The analyses show that only 0.4% of journal articles on drug studies are indexed exclusively in Embase. No added value can be determined from searching Embase.

At 97.4% and 99.5%, the proportion of MEDLINE citations in all publications considered was higher than shown in previous analyses [3,4,6,8]. This shows that drug studies are regularly published in journals indexed in MEDLINE.

CENTRAL contains the majority of the remaining studies. This is due in particular to the fact that citations from Embase, among others, are indexed in CENTRAL thanks to the efforts of the Cochrane Crowd platform (https://crowd.cochrane.org/). An analysis from 2020 confirms that Cochrane's centralized search and screening processes are highly sensitive [20]. In the present analysis, only a time delay in the indexing of older citations was found. For a search date prior to 2012 for drug reports and rapid reports (Data pool 2), 7 journal articles were included that were indexed in CENTRAL with a delay, i.e., only after the search date of the report (data not shown in the working paper). This time delay was no longer observed in more recent searches.

However, CENTRAL is not considered as a second database in a comprehensive search for non-randomized studies. Whether Embase is a suitable additional database for identifying citations not indexed in MEDLINE remains an open question for this type of study design.

The data also show that in drug studies, more than one journal article is published on a study in about 30% of cases (data not shown in the working paper). This increases the chance that at least one of the journal articles will be indexed in MEDLINE and also identified via the search. In addition, information sources such as study registries also provide references to studies and related journal articles. Compared to conducting a systematic search in Embase, a targeted search for additional publications of results is an effective alternative.

The conclusions in the analyses presented refer to journal articles. If conference abstracts are also included in the evaluation, databases such as Embase or Biosis can be an important source. This does not generally apply to IQWiG products, as since 2017 (from IQWiG's General Methods Version 5.0 onwards [21]), searches for conference abstracts have generally been dispensed with, as such documents usually contain little information on study methods and results.

It is notable that only about 80% of studies have an associated journal article. This illustrates a major change in drug assessment over the past two decades, which is largely related to the legal obligation in the US (FDA Amendments Act) and the EU (Regulation 726/2004) to register almost all clinical studies and subsequently publish the results in a registry in a timely manner. Against this background, manufacturer inquiries and searches in study registries have become

an indispensable part of systematic information retrieval, as they often contain significantly more information than publications in medical journals [22]. Journal articles are therefore often no longer the primary source of study results in the field of drug interventions.

Limitations

Due to the nature of internal data collection, only a step-by-step approach was possible for the analysis. CENTRAL and Embase citations were only considered if the respective journal article was not indexed in MEDLINE. It is therefore not possible to say whether similar coverage could be achieved with other database combinations. Given the current concerns about the reliability of US services, this question will play an important role in the future.

It should also be noted that comprehensive coverage of journal articles in a database (high coverage) does not necessarily mean that these articles are also easy to find (high recall). Consequently, the following conclusions refer to a systematic literature search in MEDLINE and CENTRAL that is designed to achieve the highest possible sensitivity. IQWiG ensures this by developing and reviewing search strategies based on predefined test sets. This process requires professional structures and in-depth expertise of information specialists in the field of information retrieval. If this expertise is not fully available, it is advisable to search additional databases – especially those with their own indexing – in order to identify relevant journal articles as completely as possible.

7 Conclusion

In the context of comprehensive information retrieval for IQWiG's benefit assessments of drugs, searching Embase in addition to MEDLINE and CENTRAL is considered unnecessary. Omitting this search is unlikely to have any consequences relevant to decision-making. A separate search in Embase does not appear to offer any relevant added value. This is particularly the case for studies initiated after 2007, when a legal requirement to register clinical trials was introduced in the United States

8 References

1. Bramer WM, Rethlefsen ML, Kleijnen J et al. Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. Syst Rev 2017; 6(1): 245. https://doi.org/10.1186/s13643-017-0644-y.

2. Ewald H, Klerings I, Wagner G et al. Searching two or more databases decreased the risk of missing relevant studies: a metaresearch study. J Clin Epidemiol 2022; 149: 154-164. https://doi.org/10.1016/j.jclinepi.2022.05.022.

3. Hartling L, Featherstone R, Nuspl M et al. The contribution of databases to the results of systematic reviews: a cross-sectional study. BMC Med Res Methodol 2016; 16(1): 127. https://doi.org/10.1186/s12874-016-0232-1.

4. Halladay CW, Trikalinos TA, Schmid IT et al. Using data sources beyond PubMed has a modest impact on the results of systematic reviews of therapeutic interventions. J Clin Epidemiol 2015; 68(9): 1076-1084. https://doi.org/10.1016/j.jclinepi.2014.12.017.

5. Aagaard T, Lund H, Juhl C. Optimizing literature search in systematic reviews - are MEDLINE, EMBASE and CENTRAL enough for identifying effect studies within the area of musculoskeletal disorders? BMC Med Res Methodol 2016; 16(1): 161. https://doi.org/10.1186/s12874-016-0264-6.

6. Metzendorf MI, Richter B, Bandeira-Echtler E et al. Descriptive analysis of non-randomized studies included in Cochrane Reviews regarding their availability in PubMed; Cochrane Colloquium, September 16-18, 2018, Edinburgh, UK [online]. 2018 [Accessed: July 28, 2025]. URL: https://docserv.uni-duesseldorf.de/servlets/DocumentServlet?id=50244.

7. Booth A. Over 85% of included studies in systematic reviews are on MEDLINE. J Clin Epidemiol 2016; 79: 165-166. https://doi.org/10.1016/j.jclinepi.2016.04.002.

8. Metzendorf M, Richter B. Selective searching for high-quality health-related evidence syntheses – more bias or time gained? Global Evidence Summit, September 13-16, 2017, Cape Town, South Africa [online]. 2017 [Accessed: July 29, 2025]. URL: https://docserv.uni-duesseldorf.de/servlets/DocumentServlet?id=50245.

9. National Library of Medicine. Medical Subject Headings 2025 [online]. [Accessed: July 28, 2025]. URL: https://meshb.nlm.nih.gov/.

10. Lefebvre C, Glanville J, Briscoe S et al. Cochrane Handbook for Systematic Reviews of Interventions; Version 6.5; Technical Supplement to Chapter 4: Searching for and selecting studies [online]. 2024 [Accessed: 29.07.2025]. URL: https://training.cochrane.org/chapter04-tech-supplonlinepdfv65270924.

11. Wong SS, Wilczynski NL, Haynes RB. Comparison of top-performing search strategies for detecting clinically sound treatment studies and systematic reviews in MEDLINE and EMBASE. J Med Libr Assoc 2006; 94(4): 451-455.

12. Higgins JPT, Lasserson T, Thomas J et al. Methodological Expectations of Cochrane Intervention Reviews (MECIR) [online]. 2023 [Accessed: 28.07.2025]. URL: https://www.cochrane.org/sites/default/files/uploads/PDFs/MECIR/MECIR%20Version_August%202023_revised%20080424.pdf.

13. Joint Federal Committee. Dossier on benefit assessment in accordance with Section 35a SGB V; Module 4; Document template [online]. 2021 [Accessed: June 25, 2025]. URL: https://www.g-ba.de/downloads/17-98-4825/2021-12-16_Anl2_6_Modul4.pdf.

14. Institute for Quality and Efficiency in Health Care. Evaluation of regular searches in the ICTRP Search Portal; working paper [online]. 2024 [Accessed: July 28, 2025]. URL: https://doi.org/10.60584/GA23-03.

15. Dobrescu AI, Nussbaumer-Streit B, Klerings I et al. Restricting evidence syntheses of interventions to English-language publications is a viable methodological shortcut for most medical topics: a systematic review. J Clin Epidemiol 2021; 137: 209-217. https://doi.org/10.1016/j.jclinepi.2021.04.012.

16. Hausner E, Sturtz S, Molnar S et al. Searching for non-English literature may be dispensable for German HTA Reports. F1000Res 2024; 13: 1134. https://doi.org/10.12688/f1000research.151365.3.

17. Novartis Pharma. Indacaterol acetate/glycopyrronium bromide/mometasone furoate (Enerzair Breezhaler); dossier for benefit assessment in accordance with Section 35a SGB V [online]. 2020 [accessed: 28.07.2025]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/577/#dossier.

18. McPartlin GM, Reynolds A, Andersen C et al. A comparison of once-daily venlafaxine XR and paroxetine in depressed outpatients treated in general practice. Primary Care Psychiatry 1998; 4(3): 127-132.

19. Institute for Quality and Efficiency in Health Care. Selective serotonin and norepinephrine reuptake inhibitors (SNRIs) in patients with depression; final report [online]. 2010 [Accessed: 28.07.2025]. URL: https://www.iqwig.de/download/a05-20a_abschlussbericht_snri_bei_patienten_mit_depressionen_v1-1.pdf.

20. Noel-Storr AH, Dooley G, Wisniewski S et al. Cochrane Centralised Search Service showed high sensitivity identifying randomized controlled trials: A retrospective analysis. J Clin Epidemiol 2020; 127: 142-150. https://doi.org/10.1016/j.jclinepi.2020.08.008.

21. Institute for Quality and Efficiency in Health Care. General methods; Version 5.0 [online]. 2017 [Accessed: July 11, 2023]. URL: https://www.iqwig.de/methoden/allgemeine-methoden_version-5-0.pdf.

22. Köhler M, Haag S, Biester K et al. Information on new drugs at market entry: retrospective analysis of health technology assessment reports versus regulatory reports, journal publications, and registry reports. BMJ 2015; 350: h796. https://doi.org/10.1136/bmj.h796.

The German version of the working paper is published under https://www.iqwig.de/projekte/ga24-04.html

Appendix A Details on journal articles indexed exclusively in Embase

Table 6: Journal articles included in dossiers and indexed exclusively in Embase

Project	Drug	Study	Study type	Included in DA (yes/no)	AN Embase	PD	Further publication (yes/no)	Registry entry (yes/no)	Manufacturer's study report[a] (yes/no)	Added value through search in Embase (yes/no)
A15-29	Edoxaban	HOKUSAI-VTE	RCT	No[b]	601778226	2014	Yes	Yes	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.
A19-58	Turoctocog alfa pegol	Pathfinder TM2	Single-arm study	No	628411208	2019	Yes	Yes	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.
A20-36	Apalutamide	SPARTAN	RCT	Yes	2004269276	2020	Yes	Yes	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.
A20-101	Tafamidis	APOLLO	RCT	No	2005630834	2020	Yes	Yes	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.[c]

a. Unpublished study report by the manufacturer.
b. Presented in dossier assessment, but no suitable study analyses are available for the benefit assessment.
c. Due to working conditions during the coronavirus pandemic, this assessment was carried out without using strictly confidential data in Module 5 of the manufacturer dossier.

AN: accession number; DA: dossier assessment; PD: publication date

Table 7: Journal articles from IQWiG reports/rapid reports that are indexed exclusively in Embase (multipage table)

Project	Research question	Study	Study type	Included in report (yes/no)	AN Embase	PD	Further publication (yes/no)	Registry entry (yes/no)	Manufacturer's study report[a] (yes/no)	Added value through search in Embase (yes/no)
A05-09	Essential hypertension	MOSES	RCT	yes	43937694[b]	2006	Yes	No	No	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.
A05-19A	Alzheimer's dementia	Anand 2000	RCT	Yes	30417804[b]	2000	No	No	No	No, as the study does not change the overall evaluation of the report.
A05-19A	Alzheimer's dementia	Cumbo 2005	RCT	Yes	43355657[b]	2005	No	No	No	No, as the study does not change the overall evaluation of the report.
A05-19A	Alzheimer's dementia	Schneider 1998	RCT	Yes	28563272	1998	No	No	No	No, as the study does not change the overall evaluation of the report.
A05-20A	Depression	McPartlin 1998	RCT	Yes	28486588[b]	1998	No	No	No	Yes
A05-20A	Depression	Smeraldi 1998	RCT	Yes	29021139[b]	1998	No	No	No	No, as the study does not change the overall evaluation of the report.
A05-20C	Depression	Halikas 1995 (003-023)	RCT	Yes	25241084[b]	1995	No	No	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.
A10-01 / A16-70b	Rheumatoid arthritis	TEMPO	RCT	Yes	38541775[c]	2004	Yes	Yes	Yes	No, as the publication language is not English or German.
A10-02	Hypercholesterolaemia	ENHANCE	RCT	Yes	358548413[b]	2010	Yes	Yes	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.

Table 7: Journal articles from IQWiG reports/rapid reports that are indexed exclusively in Embase (multipage table)

Project	Research question	Study	Study type	Included in report (yes/no)	AN Embase	PD	Further publication (yes/no)	Registry entry (yes/no)	Manufacturer's study report[a] (yes/no)	Added value through search in Embase (yes/no)
A10-03	Breast cancer	MA 17 (CFEM345G)	RCT	Yes	358316950	2010	Yes	Yes	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.
A16-70	Rheumatoid arthritis	Liu 2013	RCT	Yes	369913191	2013	No	No	No	No, as the publication language is not English or German.
A19-10	Post-meno-pausal osteoporosis	Carfora 1998	RCT	No	29137864	1998	No	No	No	No, as the study was not considered for the benefit assessment.
A19-10	Post-meno-pausal osteoporosis	FREEDOM	RCT	Yes	368549650	2013	Yes	Yes	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.
A19-10	Post-meno-pausal osteoporosis	FREEDOM	RCT	Yes	358005830	2009	Yes	Yes	Yes	No, as further publication(s) or documents on results relating to the study (e.g., study report) were identified.
A21-41	Acute coronary syndrome	CURE	RCT	No	38867645	2003	Yes	No	Yes	Study not considered for the benefit assessment.

a. Unpublished study reports from the manufacturer.
b. There is a reference to this journal article in CENTRAL, but the article was only indexed in CENTRAL after the search date for the report.
c. Journal article was included in 2 IQWiG reports.

AN: accession number; PD: publication date