PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	German primary care data collection projects: a scoping review
AUTHORS	Moser, Konstantin; Massag, Janka; Frese, T; Mikolajczyk, Rafael; Christoph, Jan; Pushpa, Joshi; Straube, Johanna; Unverzagt, Susanne

VERSION 1 – REVIEW

REVIEWER	Stausberg, Juergen University of Duisburg-Essen
REVIEW RETURNED	31-May-2023

GENERAL COMMENTS	In their scoping review, the authors identified six German projects collecting data from primary care. Going into the details, these projects reuse mainly information that had been obtained by GPs during usual care and firstly recorded in systems supporting the daily business of GP's offices (or were forgotten in the worst scenario). With this regard, the included projects do not differ from data collections summarized as „health insurance data" in the manuscript. Data were primarily recorded for purposes different from the tasks of a secondary use. Therefore, it would be appropriate to carefully consider the following aspects. A) Information is obtained by GPs, for example by taking an anamnesis or doing a physical examination. The authors could be interested in projects obtaining data in addition to usual care. Alternatively, the authors could be interested in projects that do not collect additional data but utilize data that were collected by GPs as part of usual care. B) Information could be stored anywhere firstly. Then, this information could be recorded by copying it to a second data store, or it could be entered manually a second time. Both situations do not fulfill the definition of a primary data recording. From a technical point of view, both situations implement a secondary use. With regard to A and B, the authors should clearly describe the situation they were looking for on the one hand. On the other hand, they should clarify the project's approaches. Especially inclusion criterion 2 could cause misinterpretations: „study data were routinely collected and directly extracted from PMS". For each of the six projects, the authors should describe how the projects handled the alternatives of A and B, if such information is available in the retrieved documents. Furthermore, the term EHR is misinterpreted from the reviewer's point of view. EHRs serve daily health care. If project databases are implemented for other tasks like pharmacovigilance, those data collections should be denoted as data repository, registry or observational study, not as EHR. Obviously, data repositories or registries could be filled from EHRs. However, that does not change the different use cases. As far as the reviewer understands the six

	projects, none of the data collections implemented a primary data collection in the physician offices used in daily health care. If this was the case (e.g. in case of CONTENT), the authors should clarify this use case. Overall, there are some major and minor weaknesses that should be re-thought before publication. 1. Please consider the previous, general remarks. 2. If available, please add reliability figures regarding the selection process (e. g. Kappa). 3. Table 1, frequency. Please define what is meant here by „frequency“. Please distinguish between the frequency of obtaining data in primary care (if there is one), frequency of collecting data for a single patient, frequency of storing patients in a practice and frequency of transferring data to a central data collection. 4. The reviewer asks himself whether the data collected by DA, MedVip and CONTENT could be really considered as anonymized from the point of view of the GDPR. „Anonymized“ data should be distinguished from data that do not include any direct identifier of an individual on the one hand but carry details that might allow a re-identification of a person (e. g. information about rare diseases or the job profile) on the other hand. The authors explicitly state that „MedVip project partially extracted free texts because of missing data protection regulations during that time“. This statement does not comply with the definition of MedVip as „anonymous“ in table 2. 5. The export type „pseudonymous“ is listed for BeoNet Hannover in table 2, but no respective number is given in table 1 („(-)“). 6. Table 2: Please name the export format of CONTENT. 7. Table 2: Please make clear what „upload“ means. Upload could be a function within a GP‘s practice, e. g. through a BDT transfer from the GP‘s system to another local system. But, upload could also mean the transfer of data to a central data collection. 8. The discussion suffers as well from the confusion between EHRs as tools for daily health care and data collections used for other tasks. CPRD is not an EHR: „Clinical Practice Research Datalink (CPRD) is a real-world research service supporting retrospective and prospective public health and clinical studies.“ (cf. https://cprd.com/). Please include clear definitions (as far as it is possible) for the core concepts of the manuscript. 9. It would be very interesting to know, how the cited international projects handled shortcomings of the systems that are used by GPs in daily health care. Does those shortcomings not exist in Sweden or Great Britain? Then, one could question whether it is worthwhile to invest in those systems or to invest in systems that reuse already recorded data. 10. Discussion: Informed consent is addressed in the discussion as a problem the first time. If it is so, the authors should provide information about the respective problems within the six presented projects. Otherwise, this side comment could be skipped. 11. Discussion: The authors state that “Obtaining broad consent seems to be an inevitable requirement for obtaining unstructured medical data.” The authors should explain the differences between the use of structured and unstructured data with regard to the broad consent. 12. Limitations: The authors mention “210 full-text papers”. The reviewer expected 241 full-text papers. Please correct or explain. 13. Search strings: The authors should explain, why they choose Ovid as frontend to Medline first and then Pubmed as frontend to Medline as second. Furthermore, it would be interesting for the international readership to get more information about LIVIVO. 14. PRISMA diagram: The authors mention Medline and PubMed.

	The reviewer assumes that Medline was used twice, once via Ovid and secondly via PubMed. The naming should be corrected and clarified. 15. Figure 2 is disarranged in the PDF-file. 16. Abstract, results: Please harmonize the use of absolute and relative numbers. The reviewer suggests to take 241 as 100 %. Then, each quantitative remark could be a combination like “n=23, 10%”.

REVIEWER	Hou, Bo Bradford Institute for Health Research
REVIEW RETURNED	08-Jun-2023

GENERAL COMMENTS	I read your paper with interest. I think it is a well-written paper. Two small suggestions from me, 1. Ethical considerations - it might be worth to describe this aspect of the data projects in a bit more detail. What level of consent was given in each project? e.g., for research or service improvement. 2. Maybe a bit more detail on the anonymization or pseudonymisation of the projects. How a unique patient ID was created? Can a patient have multiple unique IDs in all data projects.

REVIEWER	Nace, Travis Temple University, Temple University Libraries
REVIEW RETURNED	11-Jul-2023

GENERAL COMMENTS	This is a well done scoping review. You chose a review type that is appropriate for this type of question. The data collected is certainly unique and filling a knowledge gap for German hospitals and their EHRs. General notes: The Ovid Medline search is reproducible! Good work on this. All syntax is correct and I was able to search each line and combine appropriately. More often than not review searches are not reproducible (if included at all) Good work on the PRISMA Flow Diagram. All data is accounted for and well documented. 3. Is the study design appropriate to answer the research question? Yes but explain why a scoping review was chosen as the review type. The aim is there i.e. the question but not the reason for the study type being appropriate for the question. I believe that scoping review was the appropriate choice of review since the question is so broad and it isn't intervention based but explain why that was chosen and why it matches the question. 5. Are the methods described sufficiently to allow the study to be repeated? How was deduplication performed? The numbers are recorded in PRISMA Flow Diagram but there is no mention of the process in the search strategy portion. You need to explain how these were identified and what tools were used (if any) What tools were used for screening and data extraction? The

	process itself is mentioned but no use of tools/software to accomplish these phases. Explain how the team screened and extracted data. It says reviewed independently. Was it blinded? If so, how? The search of PubMed later in June 2022 is confusing. Explain why this was done and necessary beyond that the PI suggested it be done. Typically for evidence synthesis all searches would be done together at one time. What methodological reasoning was there to search PubMed? PubMed searches Medline as well. Was there something in PubMed that wasn't indexed in Medline that the team was concerned was missed? 13. Is the supplementary reporting complete (e.g. trial registration; funding details; CONSORT, STROBE or PRISMA checklist)? No protocol was registered for this scoping review to frame the methodology and study design. Protocol registration is seen as a vital phase of the review process including scoping reviews. Open Science Framework or another registry that accepts scoping reviews (not PROSPERO) would be appropriate for registration but this is typically done before the searches conclude. You technically could still do one but it's beyond the typical timeline that one is registered. If you don't register one I'd mention why (lack of knowledge?)

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Dr. Juergen Stausberg, University of Duisburg-Essen

Comments of reviewer 1 to the author	**Responses to the reviewer comments**
In their scoping review, the authors identified six German projects collecting data from primary care. Going into the details, these projects reuse mainly information that had been obtained by GPs during usual care and firstly recorded in systems supporting the daily business of GP's offices (or were forgotten in the worst scenario). With this regard, the included projects do not differ from data collections summarized as „health insurance data" in the manuscript. Data were primarily recorded for purposes different from the tasks of a secondary use.	**We appreciate the reviewer's valuable feedback, which has greatly improved the manuscript. The reviewer correctly points out that the identified projects primarily reuse data collected by general practitioners in electronic health records (EHRs). It's important to clarify that our scoping review focuses on all EHR data available in practice management systems, which may include vital clinical information beyond structural billing data. This distinction is essential as "health insurance data" typically covers billing information and may not capture the entirety of a patient's EHR, including lab tests and unstructured data such as reasons for encounter, medical letters, findings and information on therapies."**
Therefore, it would be appropriate to carefully consider the following aspects. A) Information is obtained by GPs, for example by taking an anamnesis or doing a physical examination. The authors could be interested in projects obtaining data in addition to usual care. Alternatively, the authors could be interested in projects that do not collect additional data but utilize data that were collected by GPs as	**We appreciate the reviewer's feedback on situations A) and B). We clarified our inclusion and exclusion criteria and write now: "1) the study population consisted of patients who received treatment from primary care physicians but could also include patients who received care from other specialists who were not considered primary care physicians; 2) use of EHR data that was initially entered into the PMS independently of primary or secondary data use; 3) data was extracted from PMS and transferred to an EHR database; 4) studies utilizing data collected as part of routine**

part of usual care. B) Information could be stored anywhere firstly. Then, this information could be recorded by copying it to a second data store, or it could be entered manually a second time. Both situations do not fulfill the definition of a primary data recording. From a technical point of view, both situations implement a secondary use. With regard to A and B, the authors should clearly describe the situation they were looking for on the one hand. On the other hand, they should clarify the project's approaches. Especially inclusion criterion 2 could cause misinterpretations: „study data were routinely collected and directly extracted from PMS".	**clinical practice; and 5) full-text publications in English or German language. The following were excluded: 1) health research studies using primary data, health insurance data, and data from disease registries; 2) conference contributions and publications in languages other than English or German; and 3) studies collecting supplementary data beyond usual care."**
For each of the six projects, the authors should describe how the projects handled the alternatives of A and B, if such information is available in the retrieved documents.	- **Regarding aspect A), we have summarized the project information by adding a new row in Table S2, titled 'Projects obtaining additional data beyond usual care.'** - **Regarding alternative B), we were unable to retrieve specific information on how the data was entered into the PMS, either fore primary or secondary use. In response to this, we have revised our inclusion criteria 2 as follows: 'use of EHR data that was initially entered into the PMS independently of primary or secondary data use.'**
Furthermore, the term EHR is misinterpreted from the reviewer's point of view. EHRs serve daily health care. If project databases are implemented for other tasks like pharmacovigilance, those data collections should be denoted as data repository, registry or observational study, not as EHR. Obviously, data repositories or registries could be filled from EHRs. However, that does not change the different use cases. As far as the reviewer understands the six projects, none of the data collections implemented a primary data collection in the physician offices used in daily health care. If this was the case (e.g. in case of CONTENT), the authors should clarify this use case.	**- We appreciate the reviewer's input regarding the interpretation of the term 'EHR.' In our introduction, we defined 'Electronic health records (EHRs)' as comprehensive records capturing health information from medical visits, which aligns with daily healthcare use.** **- We acknowledge the potential for confusion with the term 'EHR database. We want to point that this term, which we follow throughout this scoping review, is to our understanding, common terminology. A quick search on Pubmed using the key words "electronic health records database" alone identified 105 publications in which this term was used.** **- The coining of the term "EHR database" may be related to the idea that databases filled with EHR have unique characteristics. First, they collect many different variables from e.g. various disease categories. Therefore, we also dismissed the term "registry" which rather focuses on a specific disease. Even a rather specialized pharmacological database such IQVIA Disease Analyze also carries out analysis besides pharmacology including analysis of health service utilization or methodological issues surrounding EHR usage.** **- Second, as the purpose of data collection is**

	often not known in advance, we also dismissed the categorization as "observational study". In addition, some project may also use the EHR data collection infrastructure to perform interventional studies. **- Third, we therefore conclude that your suggestion of the term "data repository" would be an appropriate alternative to "electronic health records database". However, we chose to go with latter one in our review.**
Overall, there are some major and minor weaknesses that should be re-thought before publication. 1. Please consider the previous, general remarks.	**We appreciate your feedback and have carefully considered your comments, both the general remarks and specific points.**
2. If available, please add reliability figures regarding the selection process (e. g. Kappa).	**Thank you for suggesting the inclusion of reliability figures for our selection process. During the preparation of our scoping review, we followed the PRISMA-ScR checklist, which does not require the use of estimates like Kappa. We took a systematic approach to resolve differences in judgments on references, marked by Rayan, and thoroughly discussed these differences, but we did not document this process in more detail beyond what is shown in Figure 1. As a result, we do not have access to reliability figures for the selection process in our study.**
3. Table 1, frequency. Please define what is meant here by „frequency". Please distinguish between the frequency of obtaining data in primary care (if there is one), frequency of collecting data for a single patient, frequency of storing patients in a practice and frequency of transferring data to a central data collection.	**Thank you for highlighting the need for clarification regarding the term 'frequency' in Table 1. We have revised the table to use the term 'Frequency of transferring to central data collection site' in place of 'frequency.' This adjustment should provide a more precise and contextually relevant description of the data.**
4. The reviewer asks himself whether the data collected by DA, MedVip and CONTENT could be really considered as anonymized from the point of view of the GDPR. „Anonymized" data should be distinguished from data that do not include any direct identifier of an individual on the one hand but carry details that might allow a re-identification of a person (e. g. information about rare diseases or the job profile) on the other hand. The authors explicitly state that „MedVip project partially extracted free texts because of missing data protection regulations during that time". This statement does not comply with the definition of MedVip as „anonymous" in table 2.	**- We appreciate your observation regarding the distinction between anonymized and pseudonymized data, as well as the comment on the MedVip project. After careful review, we have updated Table 2 to reflect the current legislation, specifically GDPR guidelines, and have revised the Data Collection Methods section to clarify the data export types. We now write: "Anonymized data is exclusively collected by the DA and BeoNet-Halle, whereas all other projects except for the DA obtain pseudonymized data. BeoNet-Hannover, RADARplus and BeoNet-Halle have instituted informed consent procedures (Table 2)."** **- In compliance with the GDPR and the General Court of the European Union (EuG) jurisprudence (please also see: https://haerting.de/wissen/eug-zur-personenbeziehbarkeit-pseudonymer-daten/), we understand that anonymization can be considered even when there is a minimal**

	theoretical risk of re-identification, as long as this risk is legally constrained and subject to control by the data controller. **The EuGH's endorsement of this perspective aligns with our understanding that, for example, the extraction of rare diseases without direct identifiers (e.g., address or place of residence) may be classified as anonymized data, as long as re-identification would require disproportionately high criminal effort. We acknowledge the importance of this perspective in the legal context, and we have considered it in our review.**
5. The export type „pseudonymous“ is listed for BeoNet Hannover in table 2, but no respective number is given in table 1 („(-)“).	**- We appreciate the reviewer's observation regarding the export type 'pseudonymous' for BeoNet Hannover. In response to this feedback, we have taken the following actions:** **- Table 2 has been updated to reflect the 'pseudonymous' export type.** **- In Table 1, we have adjusted the numbers under the 'Total number of patients (n) per pseudonymous data category,' to 343,796**.** **- However, we wish to draw attention to a concern that has emerged during our evaluation of the data collection process for BeoNet-Hannover, as outlined in the publication at https://pubmed.ncbi.nlm.nih.gov/28697524/, as well as information verbally provided by the Principal Investigator. It has come to our attention that, for the vast majority of the 343,796 patients in the database, explicit patient consent for data usage may not have been obtained. This raises significant doubts about the GDPR (General Data Protection Regulation) compliance of the data collection process. We acknowledge that, as described in the publication, specific consent might have been collected from a limited number of patients for study-specific purposes. We have marked this as '**Marks a disagreement between our analysis and the projects principle investigator. The table indicates the statement of the principle investigator.” If there is any feedback from the reviewer on how we can make this contradiction even more understandable, we will be happy to address this.**
6. Table 2: Please name the export format of CONTENT.	**Thank you, we updated the export formats in Table 2.**
7. Table 2: Please make clear what „upload“ means. Upload could be a function within a GP‘s practice, e. g. through a BDT transfer from the GP‘s system to another local system. But, upload could also mean the transfer of data to a central data collection.	**- Thank you for pointing out the need for clarity. We revised the wording in Table 2 we have and have taken the following actions:** **- Instead of “Upload” we now use: “Medium used to upload into the central database”** **- We introduced a new row titled "Import to Database." to define whether the data is imported manually or automatically into the database.**
8. The discussion suffers as well from the	- **Thank you for your valuable feedback on the**

confusion between EHRs as tools for daily health care and data collections used for other tasks. CPRD is not an EHR: „Clinical Practice Research Datalink (CPRD) is a real-world research service supporting retrospective and prospective public health and clinical studies.“ (cf. https://cprd.com/). Please include clear definitions (as far as it is possible) for the core concepts of the manuscript.	**discussion section.** - **Above we already addressed the issue of confusion between EHRs and EHR databases. In addition, we added the following sentence in the discussion: “The findings presented in the results section shed light on the landscape of primary care data collection projects in Germany, where databases are populated with EHRs from PMS.”** - **In the revised discussion section, we now describe the Clinical Practice Research Datalink (CPRD) as follows: “The UK's Clinical Practice Research Datalink stands out as a prominent real-world research service that has contributed data to over 3,000 publications, surpassing all German projects combined by more than twelvefold (39).”**
9. It would be very interesting to know, how the cited international projects handled shortcomings of the systems that are used by GPs in daily health care. Does those shortcomings not exist in Sweden or Great Britain? Then, one could question whether it is worthwhile to invest in those systems or to invest in systems that reuse already recorded data.	**Thank you for this suggestion. To improve the discussion accordingly, we added relevant information of other countries as follows: “The results indicate that Germany ranks 16th out of 20 analyzed countries in terms of EHR implementation. This ranking places Germany behind countries like Sweden, Estonia, and the UK, which have emerged as pioneers in EHR adoption and integration (34, 35). The rapid digitalization of healthcare systems has significantly influenced the development of primary care data collection initiatives (4). It is crucial to examine the reasons behind this disparity in EHR adoption and its impact on healthcare research.** **Sweden, for example, has efficiently collected and managed patient data through an integrated system including a unique personal identity number, focusing on patient consent and supporting research and quality enhancement (36). Estonia adopted a comprehensive eHealth strategy in 2008, utilizing incentives and penalties to establish a cohesive eHealth infrastructure (37).The UK's Clinical Practice Research Datalink stands out as a prominent real-world research service that has contributed data to over 3,000 publications, surpassing all German projects combined by more than twelvefold (38). The success of these initiatives can be attributed to factors like opt-out regulations, data quality improvements, and the engagement of healthcare providers (39).”**
10. Discussion: Informed consent is addressed in the discussion as a problem the first time. If it is so, the authors should provide information about the respective problems within the six presented projects. Otherwise, this side comment could be skipped. 11. Discussion: The authors state that “Obtaining broad consent seems to be an inevitable requirement for obtaining unstructured medical data.” The authors should explain the differences between the use of structured and unstructured data	**- Thank you for this valuable feedback. We now have integrated a passage in the subsection Data collection methods where we elaborate on consent in each project as follows: “BeoNet-Hannover, RADARplus and BeoNet-Halle have instituted informed consent procedures (Table 2).** **RADARplus and BeoNet-Halle employ an adapted version of the modular Broad Consent, as per the template provided by the Medical Informatics Initiative, allowing for the transfer of identifiable data in compliance with data protection regulations {Medizininformatikinitiative, 2023 #48}. Using Broad Consent, patients have the option to provide**

with regard to the broad consent.	**consent for various modules, encompassing data collection, processing, scientific utilization of their patient data, as well as the transfer and scientific use of their health insurance data, along with the possibility for further contact. BeoNet-Hannover has introduced a study-specific consent procedure. The projects exhibit significant heterogeneity in their workflows related to data collection, transfer, and storage, including the integration of trust offices in the cases of RADARplus and BeoNet-Halle."** **- We have also integrated a subsection called Anonymization and Pseudonymization Process where we attempt to give details on the pseudonymization process.** **- We also added a paragraph in the discussin section elaborating on the use of informed consent in regard to structured and unstructured data: "Data quality is another challenge, with a predominance of free-text entries in PMS, making complete anonymization a complex task (33). EHRs encompass structured data, which is organized, quantifiable and easily analyzable due to its mostly standardized format, and unstructured data, including free-text and images. A comprehensive understanding of a patients' health history necessitates the integration of both types (3). Collaboration with the MII has introduced a Broad Consent concept that allows patients to agree to the scientific use of their data, potentially easing the extraction of free-text information in the future (26). Therefore, informed consent emerges as a vital component for advancing EHR-based research."**
12. Limitations: The authors mention "210 full-text papers". The reviewer expected 241 full-text papers. Please correct or explain.	**We updated the sentence accordingly: "Out of the 241 included publications, we retrieved full-text for 210 papers and extracted information from the abstracts for the remaining 31."**
13. Search strings: The authors should explain, why they choose Ovid as frontend to Medline first and then Pubmed as frontend to Medline as second. Furthermore, it would be interesting for the international readership to get more information about LIVIVO.	**The access to Medline via PubMed was chosen because we noticed the Ovid search missed a considerable number of articles from the IQVIA Disease Analyzer. We added a sentence explaining this in our methods section. We also added further information about LIVIVO: ""LIVIVO is a literature search portal in the field of life sciences using a semantic search technology for multiple languages including German and English. "**
14. PRISMA diagram: The authors mention Medline and PubMed. The reviewer assumes that Medline was used twice, once via Ovid and secondly via PubMed. The naming should be corrected and clarified.	- **Thank you for pointing this out and giving us the opportunity to elaborate.** - **We decided to search Medline via PubMed because after we contacted the PI of DA there was a concern that the Medline via Ovid search was missing a considerable number of publications from the DiseaseAnalyzer projects, which was confirmed by our search.** - **We also repeated the Search of Ovid Medline and LIVIVO at the same time of the PubMed search (June 2022). Due to your comment**

	we adapted the following sentence: "With encouragement from the PI of the IQVIATM Disease Analyzer, we also conducted a search on PubMed (National Library of Medicine [NLM]) using the keywords "Disease Analyzer" and "Germany" to gather all relevant publications from this database, since a considerable number of publications were identified through the PubMed search which were not previously found through the Ovid Medline search"
15. Figure 2 is disarranged in the PDF-file.	**We uploaded the file as pdf now Figure 2 should be displayed correctly**
16. Abstract, results: Please harmonize the use of absolute and relative numbers. The reviewer suggests to take 241 as 100 %. Then, each quantitative remark could be a combination like "n=23, 10%".	**Thank you, we updated the Abstract as follows: "A total of 962 references were identified, of which 291 potentially eligible studies were screened, and 241 studies based on six German EHR database projects were included. Five of the databases were publicly funded and one was privately funded. The projects showed strong heterogeneity in terms of project size, methods of data collection, and variables collected. The majority of the studies (n = 205, 85%) were contributed by only one database and most of the studies (n = 127, 52%) focused on pharmacoepidemiologic topics, including prescription patterns (n = 68, 28%) and studies about treatment outcomes, compliance, and treatment effectiveness (n = 34, 14%). Epidemiologic studies (n = 77, 32%) mainly focused on incidence and prevalence studies (n = 41, 17%) and risk and comorbidity analysis studies (n = 31, 12%). A small proportion (n = 23, 10%) of studies were in the field of health services research, such as hospitalization."**

Reviewer 2: Dr. Bo Hou, Bradford Institute for Health Research

Comments of reviewer 2 to the author	**Responses to the reviewer comments**
Hi there I read your paper with interest. I think it is a well-written paper.	**Thank you for your interest in our paper and your suggestions.**
Two small suggestions from me, 1. Ethical considerations - it might be worth to describe this aspect of the data projects in a bit more detail. What level of consent was given in each project? e.g., for research or service improvement.	**Thank you very much for this comment. We updated the subsection Data collection methods in the results section as follows: "Anonymized data is collected by the DA, BeoNet-Hannover and BeoNet-Halle, whereas all other projects obtain pseudonymized data. In order to collect pseudonymized data, BeoNet-Hannover, RADARplus and BeoNet-Halle have instituted informed consent procedures (Table 2). RADARplus and BeoNet-Halle employ an adapted version of the modular Broad Consent, as per the template provided by the Medical Informatics Initiative (MII), allowing for the transfer of identifiable data in compliance with data protection regulations {Medizininformatikinitiative, 2023 #48}. Using Broad Consent, patients have the**

	option to provide consent for various modules, encompassing data collection, processing, scientific utilization of their patient data, as well as the transfer and scientific use of their health insurance data, along with the possibility for further contact. BeoNet-Hannover has introduced a study-specific consent procedure. The projects exhibit significant heterogeneity in their workflows related to data collection, transfer, and storage, including the integration of trust offices in the cases of RADARplus and BeoNet-Halle. "
2. Maybe a bit more detail on the anonymization or pseudonymisation of the projects. How a unique patient ID was created? Can a patient have multiple unique IDs in all data projects.	**Thank you for this comment. We added a subsection "Anonymization and Pseudonymization Processes" in the results section where we provide further information on such details as follows: "We could not find publications on specific details of the anonymization process by DA. In the case of MedVip, a custom Java program in doctors' offices removes identifiable BDT fields, except for the patient ID, and encrypts BDT files {Kersting, 2010 #12}. For CONTENT, the patient's name is replaced with a unique case number before export. BeoNet Hannover generates automatic pseudonyms from patient IDs for studies, and data is pseudonymized again before leaving the practice, with data processing managed by the data manager {Lingner, 2018 #10}. RADARplus follows a privacy-by-design approach, manually documenting consented patients and separating identifiable and medical data. Identifiable data is encrypted and replaced by a pseudonym provided by a trusted third party {Bahls, 2020 #8}. For anonymized data, BeoNet Halle assigns unique 35-character keys to patients created from the patient ID which changes from export to export. For pseudonymized data, it creates temporary pseudonyms for consenting patients sent to a trusted third party for generating permanent pseudonyms, allowing data linkage across multiple sources {Moser, 2023 #50}."**

Reviewer 3: Prof. Travis Nace, Temple University

Comments of reviewer 3 to the author	**Responses to the reviewer comments**
This is a well done scoping review. You chose a review type that is appropriate for this type of question. The data collected is certainly unique and filling a knowledge gap for German hospitals and their EHRs.	**Thank you for taking the time to review our article and for the positive feedback. We are happy to read that you found our review to be a contribution to the field.**
General notes: The Ovid Medline search is reproducible! Good work on this. All syntax is correct and I was able to search each line and combine appropriately. More often than not	**Thank you for your encouraging words on our search methodology, this is very motivating for us.**

review searches are not reproducible (if included at all) Good work on the PRISMA Flow Diagram. All data is accounted for and well documented.	
3. Is the study design appropriate to answer the research question? Yes but explain why a scoping review was chosen as the review type. The aim is there i.e. the question but not the reason for the study type being appropriate for the question. I believe that scoping review was the appropriate choice of review since the question is so broad and it isn't intervention based but explain why that was chosen and why it matches the question.	**Thank you for pointing this out. We added the following sentence at the end of the introduction: "To this end, we chose to conduct a scoping review to reach, since our goal is to identify and map study characteristics and not to answer a clinically meaningful question {Munn, 2018 #49}."**
5. Are the methods described sufficiently to allow the study to be repeated? How was deduplication performed? The numbers are recorded in PRISMA Flow Diagram but there is no mention of the process in the search strategy portion. You need to explain how these were identified and what tools were used (if any)	**Thank you for this comment and the opportunity to clarify. We used EndNote to identify duplicates. However, due to different spellings not all duplicates were found through this process. Those were identified manually. We added a respective subsection "Data Management" in the method section: "The identified references were downloaded into the reference manager EndNote Version X7.8 where potential duplicates were identified with the respective tool. Duplicates that were not identified by the automated tool due to different spelling were removed manually during the review process."**
What tools were used for screening and data extraction? The process itself is mentioned but no use of tools/software to accomplish these phases. Explain how the team screened and extracted data. It says reviewed independently. Was it blinded? If so, how?	- **We added further clarification to our methods section text: "We used two online tools for systematic reviews for the screening process. Rayyan (https://www.rayyan.ai/) was used for title and abstract screening and Covidence (https://www.covidence.org/) was used for full-text screening. Both tools allow for each reviewer to decide if the text should be included, excluded or if it is undecided and to add a reason for this decision. Decisions are blinded until both reviewers are done with the screening. After both reviewers can see if they agree or disagree on the inclusion if a text."** - **We also added information on the data extraction template as follows: "Information from the retrieved publications was extracted by KM, JM, and JS. JM and JS each reviewed the included publications using a standardized data extraction template created with Microsoft Word."**
The search of PubMed later in June 2022 is confusing. Explain why this was done and necessary beyond that the PI suggested it be done. Typically for evidence synthesis all searches would be done together at one time. What methodological reasoning was there to search PubMed? PubMed searches Medline as well. Was there something in PubMed that wasn't indexed in Medline that the team was concerned was	- **Thank you for pointing this out and giving us the opportunity to elaborate.** - **We decided to search PubMed because after we contacted the PI of DiseaseAnalyzer there was a concern that the Medline search was missing a considerable number of publications from the DiseaseAnalyzer projects, which was confirmed by our search. We updated the Search in Medline via and LIVIVO at the same time of the Medline via PubMed search (June 2022). Due to your comment we added the following**

missed?	**comment to the text: "With encouragement from the PI of the IQVIA™ Disease Analyzer, we also conducted a search on PubMed (National Library of Medicine [NLM]) using the keywords "Disease Analyzer" and "Germany" to gather all relevant publications from this database, since a considerable number of publications were identified through the PubMed search which were not previously found through the Ovid Medline search".**
13. Is the supplementary reporting complete (e.g. trial registration; funding details; CONSORT, STROBE or PRISMA checklist)? No protocol was registered for this scoping review to frame the methodology and study design. Protocol registration is seen as a vital phase of the review process including scoping reviews. Open Science Framework or another registry that accepts scoping reviews (not PROSPERO) would be appropriate for registration but this is typically done before the searches conclude. You technically could still do one but it's beyond the typical timeline that one is registered. If you don't register one I'd mention why (lack of knowledge?)	**We completely agree with you. This is the first scoping review of the author group. We originally planned a systematic review and described all necessary steps under PROSPERO. Due to discussion within the author group and due to the broad review question, we changed the design at the time of our systematic search. All steps of the systematic search according to predefined inclusion/exclusion criteria, screening and data extraction are consistent with the protocol in PROSPERO.** **Not all scoping reviews contain an a priori review protocol (please refer to Munn 2018) and PROSPERO does not include protocols of scoping review, therefore, we did not cite this early registration.**

VERSION 2 – REVIEW

REVIEWER	Stausberg, Juergen University of Duisburg-Essen
REVIEW RETURNED	12-Nov-2023

GENERAL COMMENTS	The reviewer appreciates the authors' efforts to understand and to consider his concerns. Whereas the authors' rebuttal is properly presented, the changes to the manuscript are rather selective. However the manuscript improved significantly by supporting different views on the topic with its revised version. The authors correctly refer to the chaotic terminology around primary/secondary data collections and electronic records. The paper will not contribute to a clarification, but its use of this terminology might be justified by the current level of discussion, at least in Germany driven by meaningless phrases as „digitization". Furthermore, the authors clarified the understanding of „anonymized" in the identified projects. In their review, they decided to took over the projects' labelling, even if the respective definitions of „anonymization" are problematic with regard to the GDPR. Researchers often do not like to ask a patient for his or her consent. However, research should not work with misleading definitions in this situations. Research should strive for alternative legal foundations, as it was realized with the board consent mentioned in the paper.

REVIEWER	Nace, Travis Temple University, Temple University Libraries
REVIEW RETURNED	29-Nov-2023

GENERAL COMMENTS	Great work at making the corrections asked in the first round of peer review. A lot has been changed, expanded upon, and made transparent for your scoping review and how it was conducted. I appreciate the inclusion of the data extraction process and tools used in particular. This is goes a long way towards reproducibility which is what you'd want in any study and this includes evidence synthesis. I see Rayyan and Covidence were used for screening (with an explanation of the process) and Endnote was used to remove duplicates along with an explanation. While protocols aren't often required for scoping reviews it may be up to this journal and what they believe is needed/required in regards to one. They are still preferred as part of the review process and planning process for most evidence synthesis reviews. From the prior review phase I will assume there isn't one and one wasn't registered. For screening tools it isn't necessary to state 'for systematic reviews' (which this isn't). Rayyan and Covidence are used for many review types and evidence synthesis. Omit that wording and say they were used and what for. The tense is not correct in this paragraph. For example, it sounds like blinding maybe happened but with the tense used it is hypothetical that it *could* be conducted in theory. Was blinding done? Be more specific that it was done and by whom.

VERSION 2 – AUTHOR RESPONSE

Reviewer 1: Dr. Juergen Stausberg, University of Duisburg-Essen

Comments of reviewer 1 to the author	Responses to the reviewer comments
The reviewer appreciates the authors' efforts to understand and to consider his concerns. Whereas the authors' rebuttal is properly presented, the changes to the manuscript are rather selective. However the manuscript improved significantly by supporting different views on the topic with its revised version.	**Thank you for acknowledging our efforts to address your concerns. We focused on selective changes to enhance the manuscript's overall quality, prioritizing modifications with the most significant impact. We are pleased to hear that the revised version, incorporating different views on the topic, has significantly improved.**
The authors correctly refer to the chaotic terminology around primary/secondary data collections and electronic records. The paper will not contribute to a clarification, but its use of this terminology might be justified by the current level of discussion, at least in Germany driven by meaningless phrases as „digitization".	- **We have expanded the discussion section to provide further clarity on the challenges associated with the terminology of primary and secondary purposes of data collection: "An additional challenge associated with extracting data from a confusing array of modules and inter-faces within various PMS is the lack of control over the data collection, thus making it unable to ensure the quality of the data gathering process {Swart, 2015 #59}. While it seems obvious that the majority of data collected by projects serves primary purposes, encompassing information entered by physicians for patient care, billing processes,**

	or documentation requirements, there is also the possibility of data being entered for secondary purposes. Secondary purposes involves entering data for non-clinical objectives such as research, quality improvement, or public health. While data collection projects may assume a primary purpose for the collected data, in reality, such a presumption should be interpreted cautiously, especially in the context of industrial funding of health services research." - **In this context, we want to point out that our manuscript solely focuses on the purpose of data entry, not on the data collection process itself. The process of data collection can, for instance, involve direct input or copying from another source before entering it into the PMS. From our perspective, the act of data collection is distinct and independent of its intended purpose**, while the purpose represents the relevant criterion **for later analysis.** - **The revised manuscript now consistently refers to "databases populated by electronic health records from practice management systems" to eliminate any potential confusion. In response to your concern, we have removed the term "electronic health records databases" entirely.** - **We trust that these changes address your concerns and contribute to the overall clarity of our manuscript. Once again, we appreciate your time and effort in reviewing our work.**
Furthermore, the authors clarified the understanding of „anonymized" in the identified projects. In their review, they decided to took over the projects' labelling, even if the respective definitions of „anonymization" are problematic with regard to the GDPR. Researchers often do not like to ask a patient for his or her consent. However, research should not work with misleading definitions in this situations. Research should strive for alternative legal foundations, as it was realized with the board consent mentioned in the paper.	- **We appreciate the reviewer's thorough review of our work and understand the importance of clarifying the term "anonymized" in the identified projects.** - **We have reconsidered the contradiction between our analyses/results and the PI statements in the BeoNet Hannover project and opted for a more transparent presentation in Table 1 by adapting the footnote to "The table indicates reflects our findings, although we received contradictory information regarding the process and status of pseudonymization and obtaining the necessary declarations of consent for this project, so the legal status remains unclear.the statement of the principle investigatorour result." Although there are statements for this project in earlier publications of the PIs that pseudonymization and obtaining patient consent is carried out, there are also indications that this was not done.** - **We want to clarify, that our research aims to explore alternative legal foundations, as exemplified by the broad consent discussed in the paper. Additionally, we have detailed workflows in projects like RADARplus and BeoNet-Halle, showcasing the implementation of such a consent management by segregation**

	of identifiable and medical data supported by trusted third parties.
Competing interests of Reviewer: The reviewer is not really satisfied with his review of this manuscript. The paper tangles fundamental issues, but the authors missed to raise their thoughts to a level necessary to bring these issues forward. They stick to a chaotic terminology around primary/secondary data collections and electronic records on the one hand. On the other hand the authors repeat the complains of researchers concerning data privacy regulations. Especially the latter is inappropriate from the point of view of the reviewer. Unfortunately, the other two reviewers did not consider these issues in their review. Probably, both are not familiar with electronic records and privacy regulations. It should not harm the authors that they rely on existing confusions in their paper. Therefore, the reviewer will not vote for a refusal of the article. Rather, the reviewer suggest supplementing the manuscript by an editorial comment. It would by an honor for the reviewer, to formulate a respective text.	**We hope that with this revision, we could improve the manuscript to your satisfaction. We are open to you implementing an editorial comment. We appreciate your feedback and are committed to addressing any remaining concerns to ensure the quality and clarity of our work. Thank you for your continued engagement with our manuscript.**

Reviewer 3: Prof. Travis Nace, Temple University

Comments of reviewer 3 to the author	**Responses to the reviewer comments**
Hello authors, Great work at making the corrections asked in the first round of peer review. A lot has been changed, expanded upon, and made transparent for your scoping review and how it was conducted. I appreciate the inclusion of the data extraction process and tools used in particular. This is goes a long way towards reproducibility which is what you'd want in any study and this includes evidence synthesis. I see Rayyan and Covidence were used for screening (with an explanation of the process) and Endnote was used to remove duplicates along with an explanation. While protocols aren't often required for scoping reviews it may be up to this journal and what they believe is needed/required in regards to one. They are still preferred as part of the review process and planning process for most evidence synthesis reviews. From the prior review phase I will assume there isn't one and one wasn't registered.	- **Thank you for your positive feedback on our revised manuscript. We appreciate your valuable insights, especially regarding the methods section, and have invested time to address your comments.** - **Regarding the protocol, unfortunately, we did not register one, and we haven't received guidance from the journal on this matter yet. We are open to any additional suggestions or requirements the journal may have regarding protocols.** - **Your continued support and feedback are highly valued, and we look forward to further refining our work in accordance with the journal's expectations.**
For screening tools it isn't necessary to state	- **Thank you, we removed 'for systematic**

'for systematic reviews' (which this isn't). Rayyan and Covidence are used for many review types and evidence synthesis. Omit that wording and say they were used and what for. The tense is not correct in this paragraph. For example, it sounds like blinding maybe happened but with the tense used it is hypothetical that it *could* be conducted in theory. Was blinding done? Be more specific that it was done and by whom.	**reviews', as this additional information is false and irrelevant as you correctly pointed out.** - **We also changed the tense of the paragraph resulting in the following text: "We used two online tools for the screening process. Rayyan (https://www.rayyan.ai/) was used for title and abstract screening and Covidence (https://www.covidence.org/) was used for full-text screening. Both tools allow for each reviewer to decide if the text should be included, excluded or if it is undecided and to add a reason for this decision. Decisions were blinded until both reviewers were done with the screening. After both reviewers were able to see if they agreed or disagreed on the inclusion of a text."**

VERSION 3 – REVIEW

REVIEWER	Nace, Travis Temple University, Temple University Libraries
REVIEW RETURNED	30-Jan-2024

GENERAL COMMENTS	This team has made great strides to edit and modify this scoping review for publication over the last 6-7 months. The Methods section is well written, clear, and concise, and there are no lingering questions on how this review was conducted from my vantage point. The search, screening, and data analysis are well detailed and provide the how, when, where, why from a methodological standpoint. All my prior questions have been addressed. I don't have additional questions or points that need addressing at this time.