




Article

Collaborative Semantic Annotation Tooling (CoAT) to Improve Efficiency and Plug-and-Play Semantic Interoperability in the Secondary Use of Medical Data: Concept, Implementation, and First Cross-Institutional Experiences

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Featured Application: Within the context of the Medical Informatics Initiative (MII) funded by the Federal Ministry of Research and Education (BMBF), German academic medicine constructs a nationally harmonized, joint infrastructure enabling secondary use of patient data from heterogeneous clinical IT sources. The semantic annotation of such data is a prerequisite for cross-site usage. The approach and software described in and published jointly with this manuscript may not only facilitate a more efficient semantic annotation process but also promote fully interoperable semantic representations by catalyzing convergent user decisions in the presence of non-uniqueness of annotation choices.

Abstract: The cross-institutional secondary use of medical data benefits from structured semantic annotation, which ideally enables the matching and merging of semantically related data items from different sources and sites. While numerous medical terminologies and ontologies, as well as some tooling, exist to support such annotation, cross-institutional data usage based on independently annotated datasets is challenging for multiple reasons: the annotation process is resource intensive and requires a combination of medical and technical expertise since it often requires judgment calls to resolve ambiguities resulting from the non-uniqueness of potential mappings to various levels of ontological hierarchies and relational and representational systems. The divergent resolution of such ambiguities can inhibit joint cross-institutional data usage based on semantic annotation since data items with related content from different sites will not be identifiable based on their respective annotations if different choices were made without further steps such as ontological inference, which is still an active area of research. We hypothesize that a collaborative approach to the semantic annotation of medical data can contribute to more resource-efficient and high-quality annotation by utilizing prior annotational choices of others to inform the annotation process, thus both speeding up the annotation itself and fostering a consensus approach to resolving annotational ambiguities by enabling annotators to discover and follow pre-existing annotational choices. Therefore, we performed a requirements analysis for such a collaborative approach, defined an annotation workflow based on the requirement

analysis results, and implemented this workflow in a prototypical Collaborative Annotation Tool (CoAT). We then evaluated its usability and present first inter-institutional experiences with this novel approach to promote practically relevant interoperability driven by use of standardized ontologies. In both single-site usability evaluation and the first inter-institutional application, the CoAT showed potential to improve both annotation efficiency and quality by seamlessly integrating collaboratively generated annotation information into the annotation workflow, warranting further development and evaluation of the proposed innovative approach.

Keywords: semantic annotation; medical data; annotation tool; terminology; SNOMED CT; LOINC; ATC; interoperability; reusability

1. Introduction

Hospital information systems (HIS) are primarily intended for use in patient care to support the care process and enable legally required documentation. However, the patient data stored in HIS holds more value. Patient data can—if permissible by applicable privacy regulations—be utilized in secondary use scenarios, including biomedical research and quality assurance in particular [1].

Translational biomedical research using routine clinical data depends on sufficiently sized representative data sets. Researchers therefore benefit from accessing data pools from multiple organizational units such as departments, clinics, etc., which, in practical implementations of HIS that comprise multiple subsystems with heterogeneous levels of technical and organizational integration, implies merging data from various technically separate source systems. This can pose challenges even for secondary data usage within single institutions like university hospitals [2]. Effectively utilizing data across institutional boundaries is even more challenging. This challenge has been met in Germany through the Medical Informatics Initiative [3], which is funded by the Federal Ministry of Education and Research. The Medical Informatics Initiative creates national standards for patient consent [4], FHIR-based nationally harmonized clinical data representation [5], and nationally standardized contractual templates and organizational procedures to foster collaborative cross-institutional data exchange and usage [6].

While the nationally standardized interoperability specifications constrain data representation for data exchange via FHIR profiling [7] to specific terminologies or often even value sets defined as subsets of internationally standardized terminologies and ontologies to facilitate plug-and-play interoperability to the extent possible, it is difficult to map specific items from local routine clinical documentation to the relevant terminology/ontology concepts in a way that actually allows cross-institutional data usage.

This is, to a large part, due to the intrinsic ambiguity involved in annotating routine clinical data with terminologies and/or ontologies of sufficient descriptive power and scope to describe available clinical data effectively [8]. While standardized terminologies and ontologies like SNOMED CT, LOINC, and ATC [9–11] help to describe the semantics of medical data clearly and unambiguously once annotation has been performed, thus supporting cross-system and cross-institutional data use, the annotation step itself can be extremely resource intensive. Annotation calls for a rare combination of clinical, technical, and terminological expertise since it often requires the resolution of ambiguities resulting from, e.g., non-uniqueness of potential mappings to various levels of ontological hierarchies and relational and representational systems. This may require judgment calls that take into account the context of clinical data acquisition, which is typically specific to the contributing site or even organizational sub-unit, the technical consequences of specific choices, and to the extent possible, the implications of specific choices for the downstream processing and analysis steps in generic secondary use contexts. For example, Kors et al. [12] annotated biomedical data using a subset of the Unified Medical Language System [13] to provide a gold-standard of annotated data that future efforts can build upon. While a pre-annotation

step could be performed automatically, human annotators were still needed to choose from several possible annotation options and to make the final annotation choices. Currently, automatic annotation alone could not provide satisfactory results. Consequently, improving annotation workflows is an active area of research and didactic activities [14,15].

In practice, semantic annotation is often performed manually without task-specific tooling using, e.g., spreadsheet tables in combination with various online resources such as the SNOMED CT browser [16] or RELMA [17] to search the terminologies. This exacerbates the challenges outlined above and introduces additional avoidable sources of error.

Hypothesizing that innovative, task-specific annotation tooling with modern collaborative features could contribute to a more efficient and effective annotation process to support cross-site data usage scenarios, we developed a prototype of a web based, Collaborative Annotation Tool (CoAT) for the semantic annotation of medical data and evaluated its usability in intra- and cross-site application scenarios. By proposing this new collaborative approach and with CoAT providing and evaluating a prototypical implementation, we aim to both provide first evidence for the feasibility and usefulness of this approach and facilitate further research in this direction by making our solution available as open source.

2. Materials and Methods

Prototype conception and development was preceded by a systematic requirements analysis for annotation tooling. The results from the requirements analysis were formulated as user stories and grouped into “must”, “should”, and “could” requirements. Following an agile approach, the development took place in three development cycles. Each cycle focused on a defined set of user stories and produced new requirements for the next development cycle.

The web app was implemented in Java SE 11 using the Spring Boot framework as a fast and easy way to benefit from the advantages of a Spring application. Vaadin 14 was used to develop a modern web graphical user interface with Java code using the framework’s built-in UI components.

We implemented three primary features going beyond the feature set of typical tooling choices for semantic annotation.

1. Collaborative annotation: Searching for pre-existing annotations from local sites or other participating sites for fitting terminology codes as a seamlessly integrated part of the annotation process itself allows users to see what local codes from the same or other participating sites have previously been annotated using these terminology codes. Annotators can profit from comparing their local codes to other local codes previously annotated with a terminology code to determine if the terminology code is fitting based on the equivalence or similarity of the local codes under consideration.
2. Medical Data Models (MDM) portal integration: As terminologies like SNOMED CT contain hundreds of thousands of codes, many existing annotations originating from many participating sites would be needed to regularly benefit from this feature while using CoAT. To give annotators access to more input in this early pilot phase of implementation, a web service with access to annotations from the Medical Data Models portal (MDM portal) was integrated [18,19], effectively turning MDM into a large contributing annotation collaborator. The MDM portal is an online resource providing over 25,000 semantically annotated structured data acquisition forms [20], with coverage ranging from numerous electronic case report forms from clinical studies to documentation forms from clinical information systems including fully annotated versions of the 2015 state of intensive care documentation systems from both Bonn and Munster [21]. MDM integration was realized using its REST API.
3. Cross-terminology mapping: Medical ontologies and terminologies typically describe overlapping knowledge domains and are used to support different application scenarios, implying that annotating source data items with multiple semantic codes from different ontologies and/or terminologies may make annotation results more broadly applicable and practically useful. We therefore enabled CoAT to facilitate cross-/multi-

terminology annotation by seamlessly integrating the cross-terminology mapping information from the UMLS Metathesaurus [22] into CoAT for semi-automatic multi-terminology annotation.

Since only metadata but no patient specific data is to be processed, the implementation poses no risks to patient privacy if used as intended. Risks to staff privacy were minimized by limiting the processing of staff-related data items to those strictly necessary to allow for authentication and authorization of users.

The prototype was first evaluated regarding its usability in an intra-site application in Bonn. Three test users were recruited: one physician, one nurse, and one medical documenter. To evaluate the usability, these test users performed think-aloud tests [23] where they had to complete a given set of tasks in the tool that covered the whole annotation process including usage of the collaborative features. While doing so, the test users verbalized their thoughts and were recorded. The records were transcribed to document where users encountered challenges. The test lead judged users' success or failure in the completion of the tasks based on pre-defined expected results.

To evaluate the value of collaborative annotation features and pre-existing semantic annotation data in practice, the system was rolled out to two more sites in the SMITH consortium, Jena and Leipzig. At the Jena University Hospital (JUH), the Collaborative Annotation Tool was evaluated with several real-world value sets from intensive care medicine and laboratory diagnostics. Leipzig University used a real-world scenario from the MII overarching use case POLAR [24], a feasibility query selecting a number of patient's characteristics, laboratory values, and medications for evaluating the tool. In addition, the tool was also tested with medical informatics students on the same query in order to find out whether specialists without many years of expertise in medical terminology can also make meaningful initial annotations.

3. Results

3.1. Requirements Analysis

The requirements analysis resulted in functional as well as non-functional (e.g., technical) requirements for the annotation tool. Requirements were formulated and documented as user stories. The requirements analysis also established a data annotation workflow that has to be supported by the annotation tool (Figure 1).

Users are assigned the roles of administrator, annotator, or verifier according to their responsibilities for different parts of the annotation workflow. Each user, along with basic identifying data used for authentication purposes, is assigned a location identifying the site in multicentric collaborative annotation settings like those typical of the MII, where many university hospitals collaborate in and contribute to the national data sharing infrastructure. Administrators start the process by importing medical metadata, typically consisting of local item identifiers uniquely identifying the source system and data item, along with any descriptive information available from the source context, into the annotation tool using a CSV file. Imported metadata is tagged with the location of the uploading administrator to enable the display of provenance information during the annotation process and support the annotator in assessing the applicability and validity of previous annotation choices for the annotation task at hand; in addition, location assignment controls annotator and verifier work allocations—by default, annotators and verifiers are presented only with annotation tasks originating from their location. Annotators can then search terminologies for fitting codes and use collaborative features provided by the tool to annotate data uploaded to their location. Verifiers accept or deny annotations and finally, administrators can then export data with its annotations as a CSV file.

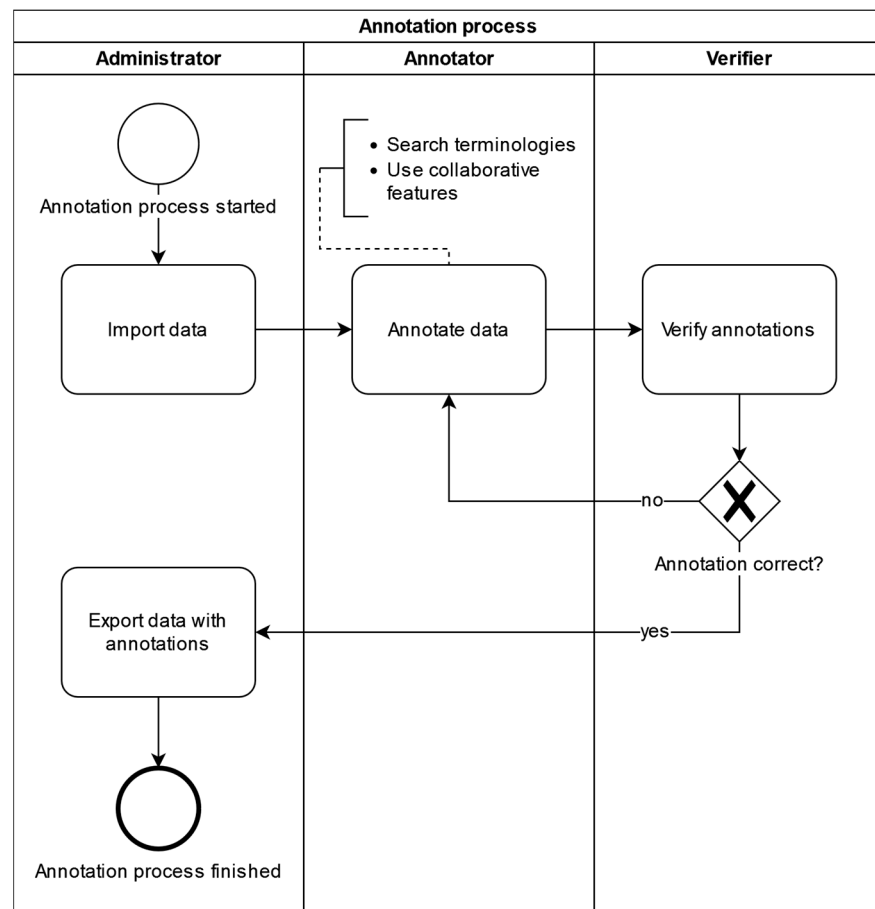


Figure 1. Data annotation workflow. Administrator, annotator, and verifier interact through the workflow management features of CoAT to produce quality assured annotations. Administrators start the annotation process by importing medical metadata into CoAT. Annotators can then search for fitting codes in standardized terminologies or use collaborative features to annotate the data. After that verifiers can either reject annotations and send them back to the annotation step for corrections or accept them. Accepted annotations can be exported by administrators for further usage, ending the annotation process.

3.2. Implementation Process and Results

Using Spring Boot and Vaadin 14 allowed for a fast implementation of a first prototype. The development of the prototype focused on the most important features of the application. At the end of the third development cycle, all “must” requirements were implemented. The application was then deployed to a virtual machine hosted by University Hospital Bonn equipped with four vCPUs and 16GB RAM, of which CoAT required less than 1GB. Based on the technologies chosen for implementation, we expect CoAT to run with sufficient performance and scalability on any typical hospital IT infrastructure.

Users with the annotator role can annotate data tagged with their location using the annotation interface (Figure 2). In the top half of the user interface (A), the actual annotation is performed. At the very top, the data to be annotated is displayed (A1). Each uploaded data item is described by an object identifier, an internal identifier—which typically identifies both the source system and data item—and a description. In the three boxes below (A2), codes from the terminologies SNOMED CT, LOINC, and ATC can be added as annotations. Further down is a line of buttons (A3) to use the cross-mapping feature and to save the annotations.

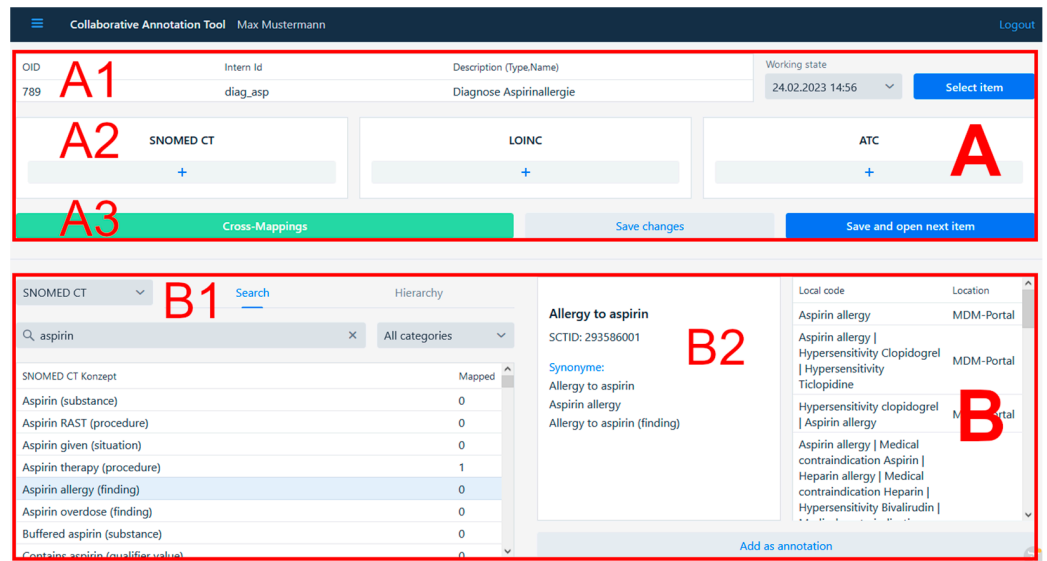


Figure 2. Annotation page. The top part of the UI (A) shows a local code (A1) that can be annotated by adding terminology codes to their respective boxes (A2) and using the cross-mapping feature (A3). The bottom part (B) displays the terminology search (B1) and detailed information on specific search results (B2).

The bottom half of the annotation, UI (B), is used to search the terminologies for fitting codes and is further divided into a left and a right part. On the left (B1), terminologies can be searched by typing in search terms or in case of hierarchical terminologies like SNOMED CT, by navigating through the tree structure defined by the hierarchy visualized using the Vaadin Tree Grid widget. Users can click on any search result to obtain detailed information from the terminology, which appears on the right (B2). On the very bottom is a button to directly add the selected search result as an annotation.

Figure 3 shows the collaborative search feature located in the bottom part of the annotation page. On the left, we can see that searching for “aspirin” in SNOMED CT yielded the result “Aspirin therapy (procedure)”, which has been used to annotate some data once before (Figure 3, B3) on the Bonn site as well as in various contexts in the MDM portal. After clicking on the search result, additional information about the search result from the source terminology as well as information about its prior usage in annotation is shown. The table on the very right (Figure 3, B4) shows which data items in which location were annotated using the selected search result. In this case, the search result was used to annotate the data item “Medication Aspirin 500 mg Tablet” at the University Hospital Bonn.

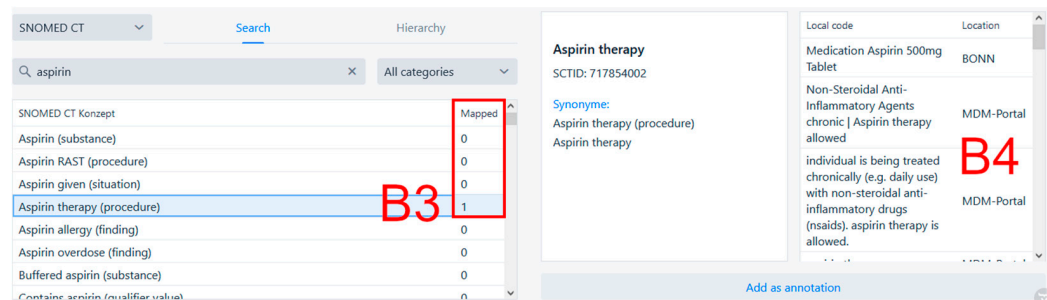


Figure 3. Detailed view of collaborative search feature. Searching terminologies yields terminology concepts with the number of times they were used as annotations (B3) as results. Selecting a single search result shows what local codes were annotated using this terminology concept including MDM portal integration (B4).

MDM integration via the REST API was achieved as planned thanks to the active support by MDM operators and provided seamless access from the annotation interface to the more than 500,000 annotated data elements available in MDM. Annotations in the MDM portal are performed using UMLS codes. To check for existing annotations in the MDM portal while searching terminologies in the Collaborative Annotation Tool, a selected search result is translated to a set of UMLS codes using the UMLS Metathesaurus. If at least one UMLS code exists, the web service of the MDM portal is called using its RESTful API and provides all data elements annotated using this set of UMLS codes. The annotated data elements from the MDM portal are added to the table with the known annotations as displayed in Figure 3.

Support for cross-terminological annotation using existing inter-terminology mappings was successfully implemented using the UMLS Metathesaurus as a mapping source. UMLS describes the medical terminology using UMLS concepts and relationships between them. A single UMLS concept describes a single medical term and contains atoms, which are codes from different terminologies that are semantically equivalent. Codes that are semantically equivalent to already annotated codes can thus be shown to the user in the CoAT UI. This feature is made accessible to the user with the cross-mapping dialogue shown in Figure 4. When a user annotates a code to a medical data item, the code is looked up in the UMLS Metathesaurus. If a UMLS concept containing this atom and other atoms from the supported terminologies is found, a button to open the cross-mapping dialogue is enabled. The dialogue shows all available semantically equivalent codes and allows the user to add them as annotations.

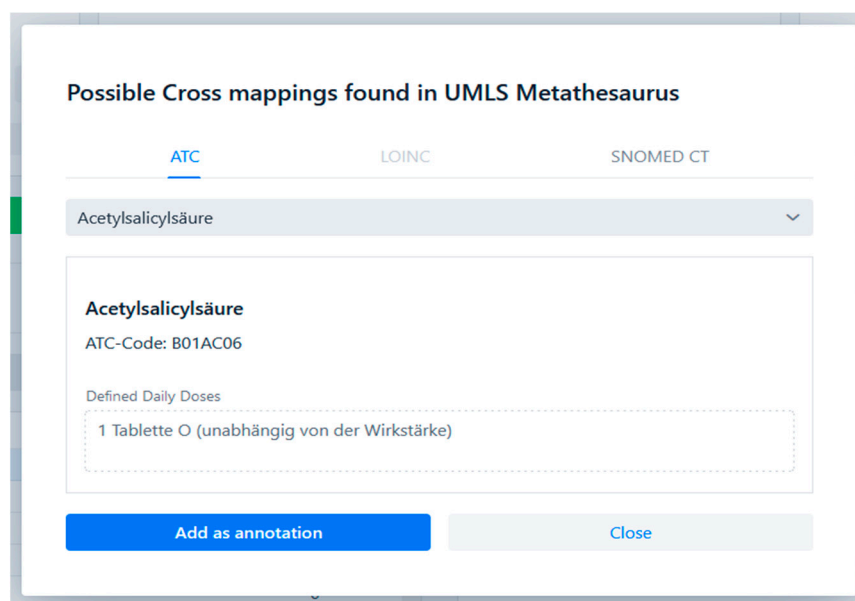


Figure 4. Cross mapping feature. The primary annotation choice, SNOMED CT concept “387458008 | Aspirin (substance)”, is mapped to ATC code “B01AC06 Acetylsalicylsäure” using the UMLS Metathesaurus terminological mapping.

3.3. Usability Evaluation

In Table 1 the results from the usability evaluation are shown. The tasks that the three test users were asked to undertake cover the key functionalities of the tool. The test users were able to successfully solve most tasks while occasionally encountering problems. The transcripts of the think-aloud tests gave additional insights about the causes of these problems and allowed us to come up with solutions to counter them. To improve the usability of the tool but not bloat the user interface, additional information to the user was made available by adding small text labels only where necessary and dialog windows that

can be opened by clicking a “help” button. Troubled users can also find help in the user guide where all key functionalities are explained.

Table 1. Usability evaluation results. Three users with different backgrounds performed nine tasks in the CoAT as part of think-aloud usability tests and were able to solve most tasks. The challenges encountered by the users were taken as input to improve the CoAT’s usability.

Task	Description	Success Rate
1.	Import data	2/3
2.	Annotate data using SNOMED CT	3/3
3.	Annotate data using LOINC	3/3
4.	Annotate data using ATC	3/3
5.	Delete a medical data item	3/3
6.	Hide an annotation	2/3
7.	Restore an older working state of an annotation	1/3
8.	Use the collaborative search feature	2/3
9.	Use the cross mappings feature	2/3

3.4. Cross-Site Evaluation

3.4.1. Evaluation at Jena University Hospital

Our goal was to map each JUH internal code from a few example value sets from intensive care medicine and laboratory diagnostics to a LOINC or SNOMED CT code. To achieve this, internal codes were inserted into a CSV file that was uploaded to the tool. The desired LOINC or SNOMED CT codes could be inserted either directly as the numerical code or by searching for, e.g., the SNOMED fully specified name and then choosing the desired code. The extraction of internal codes and the mapping was performed by a semantic interoperability specialist at JUH’s Data Integration Center. The inserted codes were previously independently validated by a physician from JUH’s Department of Anesthesiology and Intensive Care Medicine.

Using the export function, the internal codes, each now annotated with a validated international code, were exported into a .csv file. In the example shown in Table 2, eight JUH internal codes relating to ECMO and cardiac support procedures were annotated, validated, and exported. The experience with the tool gained at JUH led to systematic feedback to the developers with questions, problem fixes, and feature requests, e.g., on the provenance of internal codes, the categorizing, grouping, and commenting on annotations, exporting in the FHIR ConceptMap format, etc.

Table 2. Cross-site evaluation at Jena. Example mapping of internal codes for ECMO and heart support procedures at Jena University Hospital to SNOMED CT as received in the export from the Collaborative Annotation Tool.

Internal Code	SNOMED CT
60_va-ECMO	786451004
61_vv-ECMO	786453001
161_IABP_1:1	399217008
66_PECLA	233574002
109_vv-ECMO	786453001
109-ECMO	233573008
109_va-ECMO	786451004
109_vva-ECMO	786451004

In summary, with the test at JUH, the basic functionality and usability of the CoAT was successfully and independently verified. In addition, input from this evaluation contributed to further improvements to CoAT.

3.4.2. Evaluation at the University of Leipzig

We evaluated the tool with three different audiences, each time with the same scenario. The first group consisted of six scientists from our institute, all medical informatics specialists with experience in clinical data and medical terminology. The aim here was to see whether they could be a target group as productive users of the tool, strategically as verifiers. The second group consisted of 24 Master's students of medical informatics as part of a course on information management in clinical research in Leipzig. They had minimal prior training in the field of medical documentation and medical terminologies. We wanted to determine how well "untrained" staff could carry out initial annotation and at the same time, show the students how medical terminology is used in practice using a realistic example. The third group consisted of 75 participants in a further training course: the TMF School [25] is an annual training program run by TMF e.V. and is aimed at experienced researchers and employees in research networks. These include not only medical researchers and medical IT specialists but also project managers, bioinformaticians, lawyers, etc. In addition to the training effect, it was particularly interesting to see whether there would be any differences in the annotations compared to those of the students.

The data set to be annotated comprised 19 data elements. It was part of a genuine research project to recognize potentially inadequate medication in multimorbid patients. It is relatively simple in structure and includes demographic data, laboratory values, and medication administration. Users were provided with brief documentation on how to use the tool, and one value was annotated together as an example. The actual annotation work was scheduled to take 30 min.

As a result, users found the tool helpful and illustrative. However, not everyone was able to use it without help. The estimated time window of 30 min proved to be far too short. In addition, it was not a formal systematic evaluation. Some participants obviously used the time to playfully familiarize themselves with the available functions, as the annotations were chosen randomly. Among the "meaningful" annotations, it is noticeable that many users obviously trust the string-based search and sorting, especially for more complex terminologies. For example, the SNOMED CT concept "Age (qualifier value)" is listed prominently in the first place for "age" and was therefore selected most frequently, although other concepts like "Current chronological age (observable entity)" appeared more suitable. This was not the case for LOINC annotations, where only one person chose "43993-5 | Age at delivery" instead of "30525-0 | Age".

4. Discussion

4.1. CoAT Performance Relative to Identified User Needs and Pre-Existent Tooling

Overall, the implementation of the identified requirements proved successful. Both in formal usability, where evaluation results were comparable to previously reported evaluations of successful implementation tasks using similar implementation methodology [26,27], and cross-site evaluation with very heterogeneous user groups ranging from domain experts with additional deep terminology knowledge and experience to students in a summer school setting with no relevant prior experience, user feedback was positive. The observation that first-time users with no relevant prior experience found the annotation process challenging without further training or support appears unsurprising given the complexity of the task, independent of the tooling [28]. That even this user group was able to achieve annotation results in a relatively short time frame with multiple target terminologies appears to support the validity of the approach of providing an integrated annotation environment with workflow and cross-terminology mapping features with regard to supporting low-threshold annotation.

While still in the early prototype phase, CoAT provides good usability for complex annotation tasks and proved usable to heterogeneous user groups in a multicentric setting, suggesting that even independently from the innovative collaborative features, the further development of CoAT may provide a significant advancement over the current state of the art for the semantic annotation of medical data.

4.2. Value of Collaborative Features

The collaborative search feature allows annotators to more efficiently find search results that have previously been used for annotation by making previous annotation choices immediately transparent. Additionally, it allows annotators to compare the already annotated data items to the data item that is currently being annotated and thereby supports annotators in their judgment on whether the search results semantically fit the data item to be annotated. We believe that compared to approaches where a user actively needs to search pre-existing annotation databases to identify possibly relevant prior work, this seamless and automatic integration of pre-existing knowledge generated by collaboration partners into the annotation workflow realizes a collaboration modality adapted well to high throughput annotation workflows by implementing the communication fundamental to all collaboration implicitly and seamlessly as an integral part of the workflow itself. Nevertheless, additional support for explicit communication with collaborators may be useful and is discussed below (see Future Work).

When annotating data with codes from multiple terminologies, users have to identify (ideally) semantically equivalent codes in these different terminologies. First-time annotation for a medical data item can be challenging since precise identification of the optimal mapping of source item content in its documentation context to a terminology or possibly complex hierarchical ontology requires both medical and technical knowledge—the relationship between the medical data item and the annotation in effect corresponds to creating new knowledge by the annotator.

However, annotating other semantically equivalent codes from other terminologies after a primary annotation choice has been made in one terminology or ontology could be much easier as the relationships between codes from different terminologies stay the same, are possibly already available, and therefore may allow the user to annotate these equivalent codes. This cross-mapping feature should speed up the annotation process as it reduces the time needed to search for equivalent codes and improve annotation quality.

The collaborative features were found a welcome addition to the tool by annotators and show promise with regard to improved annotation quality, annotation consistency across sites, and decreased annotation time, but they require further evaluation.

4.3. Limitations

The usability testing was limited in scope due to resource constraints, while the results presented regarding collaborative cross-site usage are based on the first cross-site practical application of CoAT in a very limited test scenario, which in the case of the evaluation performed in Leipzig, was performed in a teaching context, preventing a more detailed statistical analysis of evaluation results. This naturally limits the generalizability of our results, which will have to be verified in larger application scenarios with direct integration into production data provisioning pipelines.

4.4. Future Work

Future research might be directed to extend the evaluation of the tool and verify the results of this paper. Further improvements to the collaborative features or the addition of new features altogether could create a larger benefit from already existing annotations including, but not limited to, supporting explicit context-aware communication with collaboration partners to enable the discussion of specific annotation challenges. As the tool is just a prototype, continued quality assurance and improvement will need to accompany further development to expand on features like supported terminologies and interoperable, bi-directional integration with production-ready data use infrastructures [29] using standardized interfaces like FHIR [30]. In particular, support for FHIR terminology services would allow for the use of central, up-to-date servers provided by maintainers and also from other terminologies than the three referenced in this paper. Equally, the feature of exporting standard formats like FHIR Concept Maps or annotating data dictionary templates from EDC systems like REDCap [31] or LibreClinica [32] directly would allow for the

integration of CoAT in routine processes. The systematic comparison of achievable annotation quality and efficiency with CoAT vs. other existing annotation tools may also provide additional insights into the differential contribution of the proposed collaborative features.

5. Conclusions

The idea of supporting semantic annotation of real world data sources by using a combination of cross-site collaborative annotation sharing integrated with both a large portal supplying annotated data sources and a metathesaurus-based cross-terminology mapping feature proved both realizable and useful. Thus, the integration of the CoAT implementation with evolving local and national level data provisioning infrastructure promises gains in both annotation efficiency and quality.

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