Converting Annotated Clinical Cases into Structured Case Report Forms

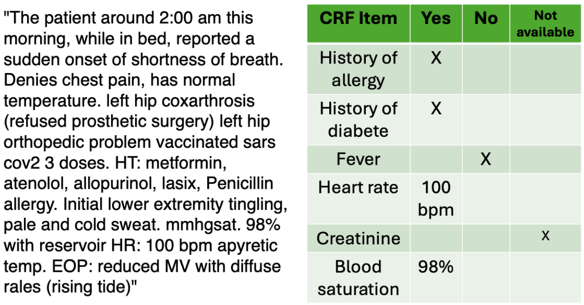
Pietro Ferrazzi[1,2], Alberto Lavelli[1], Bernardo Magnini[1],
[1]Fondazione Bruno Kessler, Via Sommarive 18, Povo, Trento, Italy,
[2] University of Padova, via Trieste 63, Padova, Italy
Correspondence: pferrazzi@fbk.eu

Abstract

Case Report Forms (CRFs) are largely used in medical research as they ensure accuracy, reliability, and validity of results in clinical studies. However, publicly available, well-annotated CRF datasets are scarce, limiting the development of CRF slot filling systems able to fill in a CRF from clinical notes. To mitigate the scarcity of CRF datasets, we propose to take advantage of available datasets annotated for information extraction tasks and to convert them into structured CRFs. We present a semi-automatic conversion methodology, which has been applied to the E3C dataset in two languages (English and Italian), resulting in a new, high-quality dataset for CRF slot filling. Through several experiments on the created dataset, we report that slot filling achieves 59.7% for Italian and 67.3% for English on a closed Large Language Models (zero-shot) and worse performances on three families of open-source models, showing that filling CRFs is challenging even for recent state-of-the-art LLMs.

1 Introduction

Case Report Forms (CRFs) are essential tools in clinical research, designed to systematically and consistently collect patient data. They are composed of a list of predefined items to be filled with patients' medical information. By standardizing data collection, they ensure accuracy, reliability, and validity, which are crucial for producing meaningful and reproducible results in clinical studies. An expanding area of research focuses on developing automated systems for filling CRFs with information extracted from clinical notes and medical records, a concept envisioned by Mac Kenzie et al. (2016) and further advanced by Gutiérrez-Sacristán et al. (2024). Leveraging Natural Language Processing methods and models represent a potentially promising approach to automate and advance research in this field. However, despite their importance, publicly available, well-annotated CRF datasets are scarce, limiting the effective development and training of such systems.



"The patient around 2:00 am this morning, while in bed, reported a sudden onset of shortness of breath. Denies chest pain, has normal temperature. left hip coxarthrosis (refused prosthetic surgery) left hip orthopedic problem vaccinated sars cov2 3 doses. HT: metformin, atenolol, allopurinol, lasix, Penicillin allergy. Initial lower extremity tingling, pale and cold sweat. mmhgsat. 98% with reservoir HR: 100 bpm apyretic temp. EOP: reduced MV with diffuse rales (rising tide)"

CRF Item	Yes	No	Not available
History of allergy	X		
History of diabete	X		
Fever		X	
Heart rate	100 bpm		
Creatinine			x
Blood saturation	98%		

Figure 1: Example of a Case Report Form filled with the values from a clinical note.

To address this gap, we propose a methodology that transforms publicly available datasets of clinical cases annotated for information extraction into a structured set of filled CRFs. Examples of such publicly available datasets are the following: MIMIC IV[1], i2b2[2], n2c2[3], CAS (Grabar et al., 2018), E3C (Magnini et al., 2023). Our approach reduces the discrepancy between existing datasets and real-world clinical needs, aligning them more closely with the practical requirements of hospitals and clinical research applications, where CRF filling is a widely relevant task. The outcome is a diverse CRF dataset, filled with information grounded in human annotations. Each example in the dataset consists of a triplet: a clinical case, a CRF to be filled, and the golden-standard filling values for the CRF derived from the clinical note, similar to what is presented in Figure 1. We apply this methodology to the European Clinical Case Corpus (E3C), release the resulting dataset, and evaluate several Large Language Models (LLMs) on it.

[1] https://physionet.org/content/mimiciv/3.1/
[2] https://www.i2b2.org/NLP/DataSets/Main.php
[3] https://n2c2.dbmi.hms.harvard.edu/

Proceedings of the 24th Workshop on Biomedical Language Processing (BioNLP 2025), pages 307–318
August 1, 2025 ©2025 Association for Computational Linguistics

The contributions of the paper are the following: (i) a general methodology for converting corpora of clinical cases annotated for information extraction into filled CRFs; (ii) a new multilingual dataset[4] (Italian and English) for CRF slot filling derived from the E3C dataset; (iii) several baselines indicating that automatic CRF slot filling from clinical notes is challenging even for state-of-the-art LLMs.

2 Related Work

Health data standardization is a fundamental aspect in the ongoing integration of medical research and artificial intelligence. To facilitate such alliance, the dimensions emphasized by Pétavy et al. (2019) are crucial, encompassing the need of health research for being transparent, accessible, interoperable, reproducible, and of high quality.

Case Report Forms play a central role in this context, and various efforts have been made to ensure that CRFs are designed to be consistent, reliable, and applicable across different clinical environments (Richesson and Nadkarni, 2011; Bellary et al., 2014). Rinaldi et al. (2025) outlines essential guidelines for CRF design, emphasizing the need to use clear, reusable, standardized, and uniquely identifiable terms to facilitate semantic consistency and future reuse. In a related line of work, Lin et al. (2015) proposes methods to ensure that CRFs are aligned with the specific research questions they aim to address, thereby reinforcing their utility and validity in clinical studies.

The shift from paper-based to electronic CRFs has been a major focus of recent research, aiming to enhance usability, reduce errors, and improve integration with digital health records (Fleischmann et al., 2017). This advancements lead to a gain of interest about automatic CRF filling from clinical reports. Mac Kenzie et al. (2016) introduced early approaches to extract structured data from narrative clinical notes, a line of research that has been extended by Gutiérrez-Sacristán et al. (2024). However, these approaches remain relatively basic, depending on keyword matching and vocabulary-based resolution, failing to leverage the full capabilities of modern Natural Language Processing techniques.

3 Methodology

In this section, we present a general methodology to convert corpora of annotated clinical cases into structured Case Report Forms. Our approach is informed by an analysis of 200 pairs of clinical notes and populated CRFs from an Italian hospital. The CRFs at hand were organized among seven key areas: patient history, clinical examination, diagnostic tests results, laboratory test results, imaging findings, treatment, and final diagnosis. While CRFs are designed to be broad and comprehensive, covering a wide range of potential clinical scenarios, an individual patient's history is typically much more limited. For this reason, we observed that in our sample the CRF items remained unfilled around 90% of the time when populated with patients' information, highlighting the general characteristic of being designed to collect much more information of what it is typically available for each specific patient.

From this analysis, we concluded that in our setup CRF design lies between two extremes: creating a unique CRF for each clinical case, leading to highly specific yet non-generalizable item sets, or crafting a single, overly broad CRF for the entire dataset, potentially blending unrelated medical domains. We adopted an intermediate approach, aligning with the traditional purpose of CRFs in clinical studies — to gather data from patients with similar conditions relevant to a study (Bellary et al., 2014). Building on this principle, we propose a two step procedure as outlined in Figure 2: in Section 3.1 we group clinical cases based on semantic similarity, and in 3.2 we generate a dedicated CRF for each group and fill it with the information annotated for each clinical note. This results in one set of CRF items per group, subsequently filled once for each clinical case in that group. To conclude, in Section 6.1 we introduce and detail the task, the evaluation metrics, and the method provided as baselines.

3.1 Clinical Cases Clustering

We aim to generate groups of clinical cases, ensuring both clinical relevance and consistency in the resulting crafted CRFs. Therefore, we require effective differentiation of documents to form clusters that group together only relevant clinical cases. If the clusters are too broad, meaningful distinctions may be lost. We prioritized diagnosis as the key

[4] The dataset is released at https://huggingface.co/collections/NLP-FBK/e3c-to-crf-67b9844065460cbe42f80166

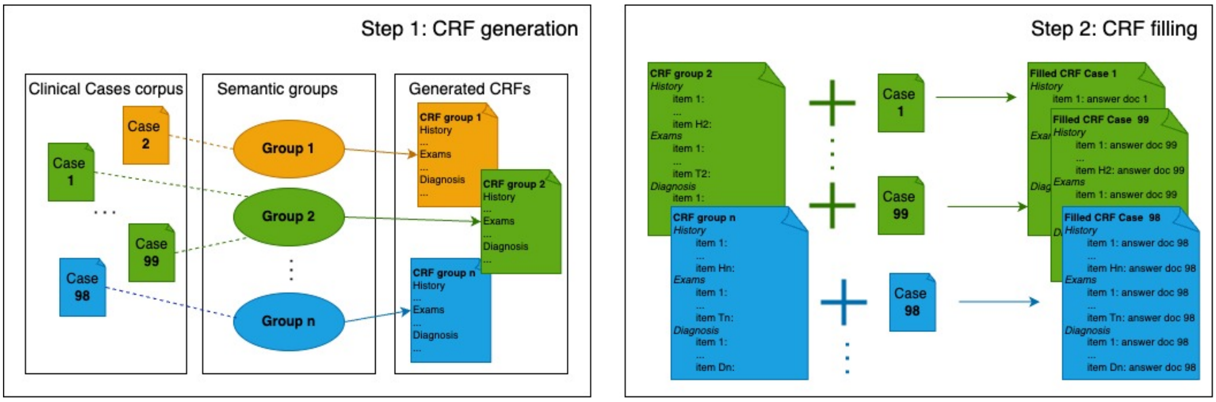


Figure 2: Summary of our two-step CRF generation and filling pipeline. **Step 1** Initially, clinical notes are clustered based on semantic similarity. Then, a group-specific CRF is generated for each cluster by extracting relevant items from the annotations of the clinical cases within the group. **Step 2** Each case is then linked to its designated CRF, which item set is populated based on the preexisting document annotation. The outcome is a list of as many CRFs as identified groups, and as many filled CRFs as documents. Each group-specific CRF is filled as many times as the number of documents belonging to it.

clustering dimension since CRF items are typically guided by the specific condition being studied. The key idea is to give significant weight to diagnosis-based links between notes in the clustering process, while retaining knowledge about entities and clinical information. Grouping documents that share similarities in these aspects helps construct synthetic CRFs that are both structured and clinically relevant.

Since many available datasets do not include explicit annotations on diagnoses, we implemented an automated system to extract them.

Diagnosis extraction. Extracting a diagnosis from a clinical note presents several challenges. Firstly, a note may mention past diagnoses that are no longer relevant. Secondly, the diagnosis might be implied rather than explicitly stated, requiring a deeper interpretation. Lastly, some clinical notes may not include a diagnosis at all, further complicating the extraction process. To address this challenge, we implement a two-step approach: *i) Automatic Generation of a Shortlist of Potential Diagnoses* – We leverage the available annotations to identify candidate diagnoses for each clinical case. First, we extract all words with the prefix "diagnos-" and check whether they are followed by an annotated entity. When this pattern was present, the associated entity is considered a potential diagnosis. Otherwise, we treat all entities in the text as potential diagnoses. *ii) Diagnosis Selection* – We refine the diagnosis by prompting a Large Language Model with the shortlist. This step outputs the exact diagnosis from the shortlist, combining the pattern-matching findings and powerful models, improving accuracy and reducing ambiguity.

Data representation for clustering. Our clustering approach is built on a graph-based representation of the data, where clinical notes are linked by weighted edges that quantify their similarity (see Figure 3 for an implementation example of such concept). This similarity is calculated based on shared entities and diagnoses across cases. A key challenge lies in the variability of how these concepts are mentioned, as the same notion can be expressed in multiple ways (e.g., “lower limb” vs. “leg", “malignant tumor” vs. “cancer"). Ensuring that notes discussing the same or closely related concepts achieve high similarity beyond mere character overlap is a critical aspect of our methodology. To address this challenge, we leveraged the UMLS Metathesaurus Names database (National Library of Medicine (US), 2024), augmenting the terms with semantically related concepts. By mean of appending to each term a short list of related ones (maximum 5), we can better capture the similarities between cases, even when different terminology is used to refer to the same or closely related clinical concepts. For languages other than English, each target mention is translated into English before performing a semantic search using a state-of-the-art language model (Zhang et al., 2025) following the findings of Chiaramello et al. (2016).

Similarity definition. To create the connection between each pair of clinical cases, we determine a similarity measure based on two components: the

ratio of shared entities (e), and diagnosis similarity (d). The ratio e is calculated as the number of UMLS-augmented shared terms divided by the number of augmented terms in the clinical note with the least of them. However, assessing diagnosis similarity d requires a different strategy due to the limited number of diagnosis terms per note. We address this using a large language model trained for semantic similarity (Lee et al., 2024), calculating cosine similarity between the UMLS-augmented diagnosis embeddings. This approach enables us to establish meaningful connections between cases, forming more coherent clusters.
We then define the overall similarity measure

$$s = 3d + e \tag{1}$$

This formulation assigns greater weight to diagnosis similarity while still preserving additional contextual information on shared entities.

Clustering. Based on the overall similarities s, we propose to apply the Louvain algorithm as described by Lu et al. (2015), selecting as starting groups the ones composed by the weakly connected sub-graphs obtained via the d edges with high weight. However, this step is highly data-dependent and must be tailored to each specific use case, following the approaches described by Xu and Tian (2015).

3.2 CRF generation

For each group of clinical notes, we aim to extract a set of relevant items for each section identified in the real-world CRFs analyzed in Section 3. The combination of the distinct section sets forms a comprehensive, group-specific CRF, tailored to the shared characteristics and clinical context of each group. Once each group-specific CRF is created, it needs to be populated for each clinical case. The overall outcome of this stage is one CRF per group and one gold-standard filled CRF per clinical case. Clinical cases within the same group share the same set of items, but their values vary based on the specific annotations present in each document.
We formulate and populate items for the identified sections, acknowledging that not all sections may be available in every dataset. As such, it is essential to determine which sections can be populated on the basis of the available annotations and, when necessary, refine the process to suit specific use cases. Here, we present an overview of the possible scenarios. *Clinical history* items can be generated using annotations such as symptom, sign, clinical entity, disease, condition, procedure. They are typically filled with positive and negative values, based on whether they occurred in the patient's past. Additionally, they may include information on whether a disease or condition is chronic or acute. *Clinical examination*, *diagnostic test results*, *laboratory test results*, and *imaging findings* can be addressed using any annotation of type similar to condition, measurement. Such items can be populated with diverse answer formats, including numerical values, categorical labels (e.g., positive/negative, high/low), and free-text descriptions, depending on the nature of the test and the information available. *Diagnosis* items can be generated based on the extraction procedure described in Section 3.1. This category of items is filled with either a positive or negative value. *Treatment* items can be addressed via labels such as medication, drug, or chemical. They can be filled with a variety of formats, spanning from medication names to time and duration information.
Initially, item sets are generated individually for each clinical note. These sets are then combined with those from other notes within the same group, forming a comprehensive and representative list of items for the entire group. Then, generated group-specific CRFs are populated for each clinical case in the group, based on the annotation, resulting in the gold-standard filled CRF.

Data revision. All generated items in each section of each group-specific CRF are normalized using UMLS mapping, collapsing equivalent terms to a single one. Furthermore, manual revision is performed to guarantee the quality of the generated CRF, with three objectives: (1) merge equivalent and highly related items, (2) remove irrelevant items, and (3) adjust inaccurate items. The process is conducted in a semi-automated manner. For each item in the CRF, we use a close source Large Language Model to assess whether it could be mapped to an existing item and to provide a justification for the suggested mapping. Any proposed mapping is manually reviewed for validity and, if approved, the overlapping items are consolidated.

4 CRF Filling: Task Definition

Datasets constructed according to the methodology detailed in Section 3.1 introduce a new CRF-filling task, which is divided into as many sub-tasks as the

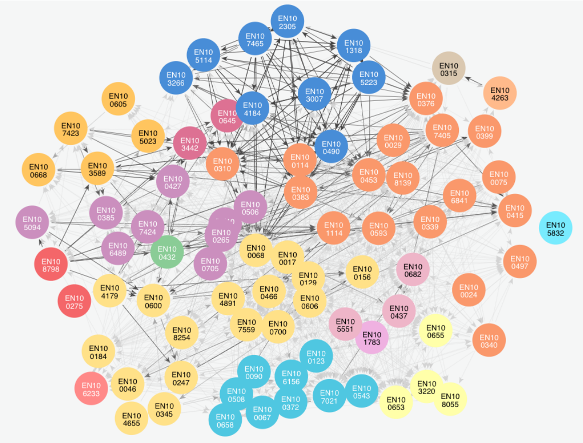


Figure 3: Graph representation of the E3C English dataset. Each node is a clinical note and the edges represent the similarity between cases. Darker edges represent higher similarity. The color of the nodes represents the group assigned by the clustering algorithm.

number of corresponding CRF sections. Each task requires filling CRF items based on information extracted from clinical cases, but they may vary in complexity. For the *diagnosis* section, the task consists in determining whether an item represents the final diagnosis, with three possible outcomes — “yes", “no", “not available". The *clinical history* section is more complex than the diagnosis one, as it allows for a broader range of valid outcomes. In addition to determining whether an event occurred in the patient’s history, it may also capture details such as its chronic or acute nature, adding an extra layer of difficulty. The *clinical examination*, *tests results*, *imaging findings* and *treatment* section are the most complex ones, as they lack a predefined set of valid answers, requiring extraction and interpretation of numerical and textual values from the clinical notes.

Baseline. We established a baseline for the CRF slot filling tasks using sequence and pattern matching techniques. For the diagnosis task, the baseline assigns “yes” if the diagnosis of interest appears in the clinical case and “not available” otherwise. In the clinical examination, tests results, imaging findings and treatment tasks, if the respective item is mentioned in the text, the first numerical value following it is extracted as the result. For the clinical history task, the baseline assigns “yes” if the corresponding textual span is found in the clinical case and “not available” otherwise.

Metrics definition. To define the evaluation metrics, we first established criteria for identifying positive and negative occurrences. An item is considered positive for diagnosis if labeled “yes” and negative if marked as “no” or “not available". In the clinical history section, an item is positive if it appears in any valid form, such as “yes” or “no", and negative if marked as “not available". For all the other tasks, an item is positive if assigned a value and negative if labeled as “not available.” Additionally, when a generated answer does not conform to the expected format—if any predefined format is required—it is always considered a false positive. Based on these definitions, we can compute task-specific precision, recall, and F_1-score, as well as overall micro and macro F_1-scores.

We apply strict matching criteria (ignoring trailing punctuation) with one relaxation: any text following “not available” in response was ignored if this phrase appeared at the beginning. For gold-standard labels filled with multiple values, a true positive (TP) is assigned for a perfect match, a false positive (FP) if extra elements are predicted, and a false negative (FN) if the prediction contains fewer items than the ground truth.

5 The Case of the E3C Dataset

In the previous sections, we outlined the general methodology for converting any corpus annotated for information extraction into gold-standard filled CRFs. In this section, we apply this methodology to the European Clinical Case Corpus (E3C, Magnini et al., 2023). E3C is an open, manually annotated multilingual dataset consisting of clinical cases in five languages. E3C clinical cases are detailed accounts of a patient’s medical history, containing rich medical details and temporal relationships that enable in-depth linguistic analysis. The dataset includes annotations on both textual spans and the relationships between them. The ones relevant to our study are summarized in Table 2. In this work, we focused on the Italian and English splits (Table 1).

5.1 CRF generation from E3C

We applied our methodology to the European Clinical Case Corpus (E3C), adapting it to the dataset’s specific characteristics. Below, we outline key adaptations, while all details not explicitly mentioned can be found in Section 3.

We generated the shortlist of potential diagnoses

Lang	# notes	# clent	# rml	# event
English	84	1024	480	4885
Italian	86	869	383	3385

Table 1: Number of clinical notes (# notes), annotated clinical entities (# clent), results and measurements (#rml), and events (# event) in E3C Italian and English splits, which both comprise approximately 25k words.

considering only clinical entities as possible targets, as other annotations were deemed out of scope. After selecting the diagnoses using GPT-4o (OpenAI and et al, 2024) in a 4-shots settings, we manually reviewed 10 examples in both English and Italian, confirming the accuracy of the results in all cases. In some instances (9 for English, 19 for Italian), no diagnosis was identified, which is expected since certain clinical documents do not report it. Then, the overall similarity measure was defined as $s = 3d + \frac{1}{2}(e + b)$, where e and b are the ratios of shared clinical entities and shared body parts respectively, d is the diagnosis similarity. The resulting graph representation of the data is shown in Figure 3. This method resulted in 7 (8) groups and 6 (12) clinical cases not assigned to any group for Italian (English). More details on the diagnosis extraction prompts, similarities and generated groups are shown in Appendix A.1 and A.3.

Using the information embedded in the E3C annotations, we formulated and populated items for the following sections: clinical history, diagnosis, clinical examination, diagnostic test results, laboratory test results, and imaging findings. Since no information on treatment was available at the annotation level, we excluded it from consideration.

Exams. To generate and populate exam items, we first extracted the textual spans linked to RMLs (results and measurements) via PERTAINS_TO relationships. A CRF exam item was created for each textual span with a corresponding RML, representing its filling value. When an RML refers to multiple textual spans, a separate item is generated for each of them. When the same textual span is associated with multiple RMLs, a single item is created for the textual span, and each RMLs is used at filling time, separated by special tokens. RMLs that do not pertain to any textual span were ignored.

Clinical History. To generate and populate items about patients history, we focused on the clinical entities enriched by three key annotated attributes: "polarity" (whether the reported term is present or not), "contextual modality" (knowledge about the truth value of the event, can be actual, hedged, hypothetical or generic), and "permanence" (can be permanent for conditions with no known cure or finite for those that can be resolved eventually). Each of these attributes defines a portion of the gold-standard answer, as outlined in Table 6 in Appendix A.2.

Diagnosis. For each diagnosis, an item was created and populated with "yes" if it applied to the clinical case and "not available" otherwise.

An example of a generated CRF can be found in Appendix A.3.

Train-test split. We adopted the train-test split provided by Ghosh et al. (2025) for the E3C dataset. The result is that clinical cases from the same group are assigned to different splits, while group-specific CRFs are generated on all the cases in the corpus. By design, CRFs must cover all essential fields for the patient groups they represent. As a result, constructing comprehensive item sets from the full dataset is necessary and does not introduce bias beyond the task's inherent structure. Crucially, only training clinical notes are used for learning, preventing any test-specific influence on the model. Note that this cross-splits effect is further reduced by creating clinical history item sets merging the ones extracted from clinical cases in both splits but excluding from the final set the ones filled only for test cases after data revision.

6 Experimental settings

We explored the E3C CRF-filling task using decoder-only Large Language Models (LLMs) as they have exhibited high performance in several tasks in zero-shot settings.

Models. We selected the instruct versions of different state-of-the-art model families, in different sizes: Llama-3 8B and 70B (et al., 2024), Qwen-2.5 7B and 72B (Qwen and et al., 2025), Mistral-Small-3.1 24B [5], Gemma-3 27B[6] and GPT 4o. This selection allowed us to compare proprietary (GPT) and open-source models (the others), assessing the impact of model size and determining which family performs better on our task. Each model was prompted with task-specific

[5] https://mistral.ai/news/mistral-small-3-1

[6] https://blog.google/technology/developers/gemma-3/

Category	Description (example)
Clinical entity	disorders, pathologies, and symptoms (“metastases” “nausea")
Body part	parts of the human body (“parotid gland")
RML	results and measurements (“38g/dl")
Event	any event (“diagnosed", “haemoglobin")
PERTAINS-TO	relation between an RML and the Event it refers to (“38g/dl” pertains-to “haemoglobin")

Table 2: E3C categories for annotations on textual spans and their relationships utilized in this work. Each textual span is annotated if it represents a clinical term (i.e., clinical entities such as pathologies and symptoms, body parts, laboratory tests and results) and is assigned some attributes. For more details, see Magnini et al. (2023).

			Italian		**English**	
Task	**Description**	**Accepted answers**	Train **Items (Filled)**	Test **Items (Filled)**	Train **Items (Filled)**	Test **Items (Filled)**
Diagnosis	determine if an item is the final diagnosis for the patient	“yes", “no", “not available”	498 (8%)	553 (7%)	491 (9%)	505 (9%)
History	determine whether the patient experienced a history item	“Certainly yes", “No", "Probably yes, chronic", “not available” etc.	977 (23%)	903 (11%)	953 (25%)	872 (13%)
Exams	extract the results related to an exam item	any string representing an exam result	1108 (10%)	1149 (10%)	984 (11%)	916 (9%)
Total			**2583 (14%)**	**2605 (10%)**	**2428 (16%)**	**2293 (11%)**

Table 3: Description, space of possible answers, number of items, and ratio of populated items in the train and test splits for both languages for the three CRF sub-tasks. All three sub-tasks are quite sparse, with around ten to fifteen percent of the items populated in the gold-standard filled CRFs. Clinical notes in the train and test split are composed by around 12k and 13k tokens (words), respectively, in both Italian and English. The possible answers for history are determined by the levels of the annotated attributes utilized for the gold-standard filling.

Model	**Diagnosis**			**History**			**Exams**			**Micro**	**Macro**
	Prec	Rec	F_1	Prec	Rec	F_1	Prec	Rec	F_1	F_1	F_1
Baseline	64.9	58.5	61.5	100.0	11.3	20.4	13.6	10.8	12.0	31.3	25.4
Llama 8B	32.2	92.7	47.8	7.2	60.8	13.0	4.8	25.0	8.1	23.0	18.2
Qwen 7B	72.1	75.6	73.8	33.8	73.6	46.4	7.5	8.5	7.9	42.7	35.2
Mistral 24B	68.4	63.4	65.8	51.6	64.9	57.5	13.8	22.1	16.9	46.7	41.4
Gemma 27B	73.5	87.8	**80.0**	47.1	83.5	60.2	22.9	83.9	36.0	58.7	53.7
Llama 70B	54.7	100.0	70.7	32.8	77.3	46.0	16.0	67.8	25.9	47.5	42.4
Qwen 72B	75.6	75.6	75.6	58.1	74.2	**65.2**	19.4	38.7	25.8	55.5	50.0
GPT 4o	75.6	82.9	79.1	40.8	75.3	52.9	34.0	76.8	**47.1**	**59.7**	**55.9**

Table 4: Performance of different models on the Italian dataset across three categories: Diagnosis, History, and RML. Metrics include Precision, Recall, F_1-score. Overall micro and macro F_1-scores are also reported.

Model	Diagnosis			History			Exams			Micro	Macro
	Prec	Rec	F_1	Prec	Rec	F_1	Prec	Rec	F_1	F_1	F_1
Baseline	84.6	53.7	65.7	87.5	13.2	23.0	0.0	0.0	0.0	29.6	21.9
Llama 8B	49.3	94.9	64.9	10.2	76.4	18.0	6.4	63.0	11.6	31.5	25.1
Qwen 7B	100.0	63.4	77.6	40.0	78.4	53.0	15.6	16.3	15.9	48.8	41.9
Mistral 24B	63.6	80.0	70.9	55.3	68.9	**61.3**	22.7	62.5	33.3	55.2	51.0
Gemma 27B	91.4	78.0	84.2	42.9	74.5	54.5	32.7	86.0	47.4	62.0	57.7
Llama 70B	84.2	78.0	81.0	36.1	74.3	48.6	34.8	81.6	48.8	59.5	55.6
Qwen 72B	96.8	73.2	83.3	55.9	67.0	60.9	27.0	80.0	40.3	61.5	56.6
GPT 4o	94.4	82.9	**88.3**	47.5	72.4	57.4	42.2	84.3	**56.2**	**67.3**	**63.4**

Table 5: Performance of different models on the English dataset across three categories: Diagnosis, History, and RML. Metrics include Precision, Recall, and F_1-score. Overall micro and macro F_1-scores are also reported.

details, the clinical case, the CRF item, and answering guidelines.

All experiments on open-source models were run on 8xA40 (46GB) and took approximately 30 GPU hours, serving the models using the vllm package (Kwon et al., 2023). Prompts can be seen in detail in Appendix A.4.

6.1 CRF Filling from E3C Clinical Cases

The constructed dataset introduces a new E3C CRF-filling task, which is divided into three sub-tasks: clinical history, exams, and diagnosis as described in Table 3. The main specialty of this task in respect to the more general outlined in Section 4 is that clinical history items can be filled with twelve valid values (Appendix A.2). Given the unique annotation scheme in E3C, which includes multiple levels of polarity, contextual modality, and permanence, such complexity is specific to this dataset and may not be present in others. Therefore, we report results on a simplified version where all positive responses are grouped as “yes” and all negative ones as “no". By simplifying the values, we aim to offer a more general perspective on the inherent difficulty of the task, extending beyond the particularities of the E3C dataset.

7 Results and Discussion

Experimental results are reported in Tables 4 and 5 for Italian and English respectively. GPT-4o consistently achieves the highest overall performance in both Italian and English datasets, with the best Micro and Macro F_1-scores (59.7 and 55.9 for Italian, 67.3 and 63.4 for English). Among open-weight models, Gemma 27B and Qwen 72B perform competitively in Italian, closely approaching GPT-4o's results, particularly in diagnosis and history. For English, Gemma 27B, Qwen 72B, and Llama 70B performances are very similar, around 6-8 points lower than GPT-4o.
Regarding model size, we observe an average improvement of around 20 Macro F_1 points when scaling from small (7/8B) to large (70/72B) models in the LLaMA and Qwen families. Interestingly, models in the 20–30B range often match or surpass larger ones from different architectures. Among the tasks, exams prove to be the most challenging, followed by history, indicating significant room for improvement. Models perform on average better on English than in Italian with no exception, with an average delta of 7.5 points of Micro F_1. Among the smaller models, Qwen 7B significantly outperforms Llama 8B, which struggles with extremely low precision. At larger scales, Qwen 72B and Llama 70B exhibit comparable performance in English, while Qwen 72B demonstrates a clear advantage over Llama 70B in Italian.

8 Conclusion

Our study presents a novel methodology for transforming annotated clinical notes into structured Case Report Forms (CRFs) by leveraging clusters of semantically similar cases. This approach ensures that CRFs are both comprehensive and contextually relevant while maintaining consistency across similar clinical scenarios. Given the scarcity of publicly available CRF datasets, our method provides a valuable framework for automating CRF generation, which could be highly beneficial for future clinical applications. In addition, our method brings existing datasets closer to real-world clinical applications, ensuring greater alignment with the practical needs of hospitals and research. Given that CRF filling is a widely relevant task, this approach enhances the utility of annotated clinical notes.

Our findings highlight that the characteristics of the generated CRFs are strongly influenced by the dataset's distribution, underscoring the necessity of manual tuning based on available annotation types when adapting the method to different contexts. We believe that a robust analysis of the data distribution is crucial for high-quality CRF generation.

Our experimental results reveal that the constructed CRFs encompass tasks of increasing complexity for state-of-the-art models. Diagnosis items can be framed as a relatively straightforward binary classification task, while history items remain within a classification framework but with greater difficulty due to their nuanced nature. The most challenging aspect lies in handling exams, tests, and examinations, which require a fully generative approach without a predefined set of valid responses, making them particularly difficult for current models to solve. Both open- and closed-source models show room for improvement in terms of performance.

Limitations

There are a few limitations in our current approach to convert Information Extraction datasets into structured CRFs. First, the proposed methodology has been experimented only on the E3C corpus: although this is a significant use case (several levels of annotations, several languages), additional insights may derive from different available datasets. Second, in order to keep under control our experimental setting, we made a few simplifications with respect to the full complexity of the task. Particularly, for the CRF *clinical history* group, we assumed a three-value schema (i.e., a certain clinical evidence is either present, negated, or not mentioned), while in reality the possible values should be extended to cover cases of chronicity.

Acknowledgments

This work has been partially funded by the European Union under the Horizon Europe eCREAM Project (Grant Agreement No.101057726) and IDEA4RC Project (Grant Agreement No.101057048). Views and opinions expressed are however those of the authors only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.

References

Shantala Bellary, Binny Krishnankutty, and M. S. Latha. 2014. Basics of case report form designing in clinical research. *Perspectives in Clinical Research*, 5(4):159–166.

Emma Chiaramello, Francesco Pinciroli, Alberico Bonalumi, Angelo Caroli, and Gabriella Tognola. 2016. Use of "off-the-shelf" information extraction algorithms in clinical informatics: A feasibility study of MetaMap annotation of Italian medical notes. *Journal of Biomedical Informatics*, 63:22–32.

Aaron Grattafiori et al. 2024. The Llama 3 herd of models. *Preprint*, arXiv:2407.21783.

Robert Fleischmann, Anne-Marie Decker, Antje Kraft, Knut Mai, and Sein Schmidt. 2017. Mobile electronic versus paper case report forms in clinical trials: a randomized controlled trial. *BMC Medical Research Methodology*, 17(1):153.

Soumitra Ghosh, Begona Altuna, Saeed Farzi, Pietro Ferrazzi, Alberto Lavelli, Giulia Mezzanotte, Manuela Speranza, and Bernardo Magnini. 2025. Low-resource information extraction with the European Clinical Case Corpus. ArXiv preprint.

Natalia Grabar, Vincent Claveau, and Clément Dalloux. 2018. CAS: French corpus with clinical cases. pages 122–128, Brussels, Belgium. Association for Computational Linguistics.

Alba Gutiérrez-Sacristán, Simran Makwana, Audrey Dionne, Simran Mahanta, Karla J. Dyer, Faridis Serrano, Carmen Watrin, Pierre Pages, Sajad Mousavi, Anil Degala, Jessica Lyons, Danielle Pillion, Joany M. Zachariasse, Lara S. Shekerdemian, Dongngan T. Truong, Jane W. Newburger, and Paul Avillach. 2024. Development and validation of an open-source pipeline for automatic population of case report forms from electronic health records: a pediatric multi-center prospective study. *eBioMedicine*, 108. Doi: 10.1016/j.ebiom.2024.105337.

Woosuk Kwon, Zhuohan Li, Siyuan Zhuang, Ying Sheng, Lianmin Zheng, Cody Hao Yu, Joseph E. Gonzalez, Hao Zhang, and Ion Stoica. 2023. Efficient memory management for large language model serving with PagedAttention. In *Proceedings of the ACM SIGOPS 29th Symposium on Operating Systems Principles*.

Chankyu Lee, Rajarshi Roy, Mengyao Xu, Jonathan Raiman, Mohammad Shoeybi, Bryan Catanzaro, and Wei Ping. 2024. NV-Embed: Improved techniques for training LLMs as generalist embedding models. *Preprint*, arXiv:2405.17428.

Ching-Heng Lin, Nai-Yuan Wu, and Der-Ming Liou. 2015. A multi-technique approach to bridge electronic case report form design and data standard adoption. *Journal of Biomedical Informatics*, 53:49–57.

Hao Lu, Mahantesh Halappanavar, and Ananth Kalyanaraman. 2015. Parallel heuristics for scalable community detection. *Parallel Computing*, 47:19–37.

W. R. Mac Kenzie, A. J. Davidson, A. Wiesenthal, J. P. Engel, K. Turner, L. Conn, S. J. Becker, S. Moffatt, S. L. Groseclose, J. Jellison, J. Stinn, N. Y. Garrett, L. Helmus, B. Harmon, C. L. Richards, J. R. Lumpkin, and M. F. Iademarco. 2016. The promise of electronic case reporting. *Public Health Reports*, 131(6):742–746. Epub 2016 Oct 13.

Bernardo Magnini, Begoña Altuna, Alberto Lavelli, Anne-Lyse Minard, Manuela Speranza, and Roberto Zanoli. 2023. *European Clinical Case Corpus*, pages 283–288. Springer International Publishing, Cham.

National Library of Medicine (US). 2024. UMLS knowledge sources [dataset on the internet]. release 2024aa. Cited 2025 March.

OpenAI and Josh Achiam et al. 2024. Gpt-4 technical report. *Preprint*, arXiv:2303.08774.

Frank Pétavy et al. 2019. Global standardization of clinical research data. *Applied Clinical Trials*, 28(4):20–23.

Qwen and An Yang et al. 2025. Qwen2.5 technical report. *Preprint*, arXiv:2412.15115.

Rachel L. Richesson and Prakash Nadkarni. 2011. Data standards for clinical research data collection forms: current status and challenges. *Journal of the American Medical Informatics Association*, 18(3):341–346.

Eugenia Rinaldi, Caroline Stellmach, and Sylvia Thun. 2025. How to design electronic case report form (ecrf) questions to maximize semantic interoperability in clinical research. *Interactive Journal of Medical Research*, 14:e51598.

Dongkuan Xu and Yingjie Tian. 2015. A comprehensive survey of clustering algorithms. *Annals of Data Science*, 2(2):165–193.

Dun Zhang, Jiacheng Li, Ziyang Zeng, and Fulong Wang. 2025. Jasper and Stella: distillation of SOTA embedding models. *Preprint*, arXiv:2412.19048.

A Appendix

A.1 Diagnosis Extraction

Here we report the structure of the prompt utilized to generate the diagnosis using GPT-4o:

```
{System prompt}{Example 1}...{Example 4}
"clinical note":{Clinical case}
"potential diagnosis":
{list of potential diagnosis}
```

Here is the system prompt:

```
You are a clinical assistant.
Your job is to extract the conclusive
diagnosis from a clinical note written by
an experienced physician.
The diagnosis is a medical condition
identified by a health care provider.
To complete the task, you are aided by a
list of possible diagnoses.
Here are your guidelines:
1. The diagnosis is always contained in
the list of potential diagnoses.
2. Your goal is to extract only the
diagnosis, ignoring everything else.
3. Respond with a json containing the
extracted diagnosis and a short motivation
{“motivation”: “motivation for the
extracted diagnosis”, “diagnosis”:
“extracted diagnosis”}.
4. If no diagnosis is reported,
respond with “no diagnosis.”

CAUTION: Notes may contain diagnoses
made in the past with respect to
the current clinical situation.
Only extract diagnoses related to
the current situation.
```

Table 7 presents examples of similarity scores for E3C cases calculated in the embedding space of the diagnosis augmented via UMLS semantic search.

A.2 E3C Clinical History Items

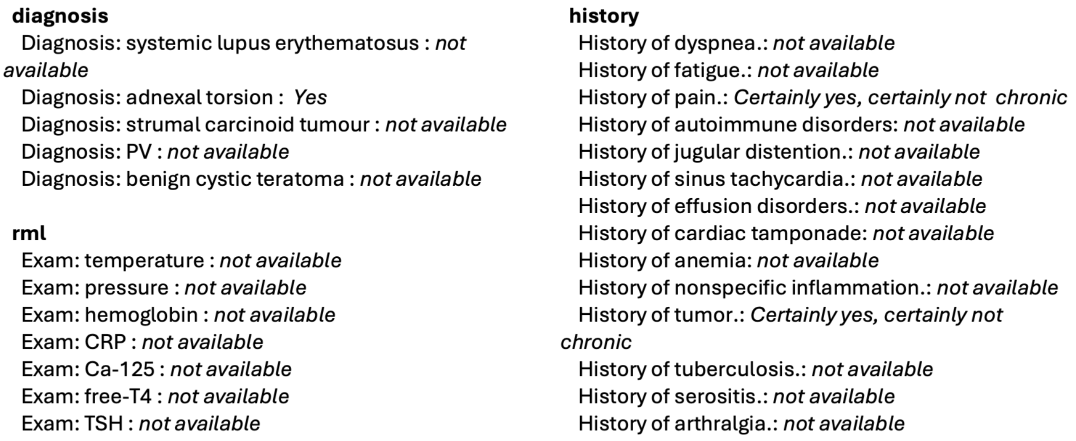
Table 6 reports the attributes and their levels used for populating the E3C CRF clinical history section. Each E3C clinical entity is annotated with contextual modality, polarity, and permanence, which determine the filled value using the template:

```
{contextual mod} {polarity}, {permanence}
```

For instance, an entity with polarity “positive", contextual modality “hedged" and permanence “finite" is filled with “Probably yes, possibly chronic". There are 12 possible level combinations.

A.3 Generated E3C CRFs

Table 8 presents the statistics on the generated E3C CRF for English and Italian. Figure 4 shows an example of a CRF generated for the English group 1.



diagnosis

Diagnosis: systemic lupus erythematosus : *not available*

Diagnosis: adnexal torsion : *Yes*

Diagnosis: strumal carcinoid tumour : *not available*

Diagnosis: PV : *not available*

Diagnosis: benign cystic teratoma : *not available*

rml

Exam: temperature : *not available*

Exam: pressure : *not available*

Exam: hemoglobin : *not available*

Exam: CRP : *not available*

Exam: Ca-125 : *not available*

Exam: free-T4 : *not available*

Exam: TSH : *not available*

history

History of dyspnea.: *not available*

History of fatigue.: *not available*

History of pain.: *Certainly yes, certainly not chronic*

History of autoimmune disorders: *not available*

History of jugular distention.: *not available*

History of sinus tachycardia.: *not available*

History of effusion disorders.: *not available*

History of cardiac tamponade: *not available*

History of anemia: *not available*

History of nonspecific inflammation.: *not available*

History of tumor.: *Certainly yes, certainly not chronic*

History of tuberculosis.: *not available*

History of serositis.: *not available*

History of arthralgia.: *not available*

Figure 4: Example of a generated CRF for English group 1 and filled with the annotation from the clinical case EN100668

Attribute	Level	CRF Value
Polarity	Positive	Yes
	Negative	No
Modality	Actual	Certainly
	Hypothetical	Possibly
	Hedged	Probably
	Missing	(empty)
Permanence	Permanent	Chronic
	Finite	Certainly not chronic
	Missing	Possibly chronic

Table 6: Attribute levels for populating the E3C CRF clinical history section.

A.4 Prompts for experiments

The prompt for the experiments is composed following this template:

`{system prompt} {answering guidelines} {clinical case} {question on the item}.`

Here we report the prompts used for English. The ones for Italian are the direct translation of them.

System prompt

```
You are an expert clinical doctor. You have
to answer a question on "{task_description}"
about a patient. To do it, you are given
the patient clinical history.
```

History answering guidelines , where values are populated according to the logic presented in the methodology section.

```
The answer is composed by three components:
polarity, contextual modality, and
permanence. You must combine these
three components together to answer
the question.
- contextual modality can be:
a)'VALUE_1' if the answer is certain,
b)'VALUE_2' if the answer is hypothetical,
c)'VALUE_3' if the answer is probable.
- polarity can be:
a)'VALUE_4' if the answer is affirmative,
b)'VALUE_5' if the answer is negative.
- permanence can be:
a)'VALUE_6' if the object of the question
is certainly permanent forever,
b)'VALUE_7' if the object of the question
is temporary or transitory,
c)'VALUE_8' otherwise.

These three components must be combined
in order: "contextual modality polarity,
permanence". For example, if the question
is "Does the patient have a history of
diabetes?", the answer could be:
"EXAMPLE_1", or "EXAMPLE_2".

If the information is not contained in
the clinical history, answer with
'not_available'.
Do not add any preamble to the answer.
```

Exams answering guidelines

```
The answer can assume three different
formats.
-if the test/exam has been performed
only once, answer with the results
of the test/exam.
```

Diagnoses note 1	Diagnoses note 2	Similarity Score
neuroendocrine neoplasia	neoplasia	0.63
chronic myeloid leukemia Ph+ in chronic phase	JMML	0.57
acute ulcerative rectocolitis	clostridium difficile colitis	0.58
mass of tumor origin	syncopal episodes, Polymorphic ventricular tachycardia	0.11
Wilms's tumor, Metastasis	microperforation	0.10

Table 7: Similarity scores between extracted diagnoses for pairs of clinical cases. The first three lines represent cases with high similarity, while the last two cases with low similarities. It can be noted that terms that are syntactically different but semantically close such as "JMML" and "Chronic myeloid leukemia Ph+ in chronic phase" are mapped together by this approach, as the former has been correctly enriched with the term "juvenile myeloid leukemia", that results in an embedding similar to the latter. At the same time, cases with very different diagnoses are assigned very low similarities.

Italian					English				
Group	Cases Train/Test	CRF items	Avg/StDev (Train)	Avg/StDev (Test)	Group	Cases Train/Test	CRF items	Avg/StDev (Train)	Avg/StDev (Test)
0	4/4	23	5.5 / 2.2	5.5 / 0.8	0	7/2	71	11.7 / 4.7	5.0 / 3.0
1	11/13	91	7.9 / 5.3	7.9 / 3.6	1	1/4	26	19.0 / 0.0	3.0 / 1.2
2	4/4	55	13/ 9.7	13 / 2.2	2	1/1	10	6.0 / 0.0	4.0 / 0.0
3	2/7	27	4.5 / 1.5	4.5 / 2.7	3	3/6	54	11 / 9.7	6.8 / 5.2
4	4/6	76	9.8 / 4.8	9.8 / 9.2	4	5/4	24	3.6 / 1.5	4.0 / 2.5
5	4/4	48	9.8 / 7.8	9.8 / 4.5	5	9/9	99	11 / 7.7	7.9 / 4.0
6	9/4	79	12.7/ 7.5	13 / 1.2	6	8/9	36	9.0 / 4.0	7.0 / 5.1
					7	2/2	75	9.4 / 5.4	13 / 11

Table 8: Number of cases, number of items, average and standard deviation of the number of populated items (i.e., different from "not available") per group-specific CRF for both languages.

```
-if the test/exam has been performed
 more than once, report all the
 results separated by the special
 token  [\MULTI_ANSWER]  (for example
 "RESULT_1 [\MULTI_ANSWER] RESULT_2").
-if the information is not contained in
 the clinical history, answer
 with 'not_available'
```

Diagnosis answering guidelines

```
Answer 'Yes' if the patient's definitive
diagnosis is the one indicated. If the
information is not contained in the
clinical history, answer with
'not_available'.
```

Question structure for exams

```
What are the results and measures of {item}?
```

Question structure for diagnosis

```
Is the definitive diagnosis {item}?
```

Question structure for history

```
Does the patient have a history
of {item}?
```