eCREAM
enabling Clinical Research
in Emergency and Acute care Medicine

STUDY PROTOCOL

Propensity to hospitalize patients from the ED in European centers

An observational retrospective quality-of-care study

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SUMMARY

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SYNOPSIS

BACKGROUND AND RATIONALE	Hospital admission rates from emergency departments (EDs) vary widely, not only because of the differences in case mix. Inappropriate hospitalization is an important factor of such variability, and it negatively affects patients and hospitals. Thus, improving the appropriateness of admitting patients is a primary public interest. Allowing centers to compare their performance with other centers, adjusting for case mix and context, is a proven approach that leads to improvement. Such comparison requires statistical models capable of accurately estimating patients' admission probability as a function of patients and ED characteristics. Unfortunately, the models proposed in the literature are based on vague representations of patients' conditions, basically those available in administrative databases. The impossibility of relying on dedicated data collection due to the vast number of patients treated in the ED and the chronic shortage of staff in these services has greatly limited the availability of accurate and reliable data. The only solution to fill the gap between the need for research and the availability of high-quality data is to extract them directly from the electronic health records (EHRs) of the EDs.
OBJECTIVES OF THE STUDY	To develop two statistical models to estimate the propensity to hospitalize patients arriving at the ED with dyspnea or after transient loss of consciousness (TLoC). IT solutions developed in the eCREAM project will be used to obtain high-quality structured data from ED EHRs. A secondary objective is to study the association between the adjusted hospitalization rate and 30-day mortality.
STUDY DESCRIPTION	Observational, multicenter, retrospective study that will last 24 months. 30 EDs from Italy, Poland, Slovakia, Slovenia, Switzerland, and the UK will participate. Data on all patients who attended the ED between 2021 and 2023 will be collected. Three types of information will be collected: 1) structural organizational data, 2) transient organizational data, and 3) data on patient characteristics upon arrival at the ED. Type 1 data will be collected at the individual center level, type 2 data will be collected on all patients who attended the ED, type 3 data will be collected only on patients with dyspnea or TLoC. The latter two will be obtained automatically from the EHRs of the participating EDs.
STATISTICAL ANALYSIS	A multivariable statistical model will be used to estimate the probability of hospitalization. Through the model, the standardized hospitalization rate, an adjusted indicator of the center's own propensity to hospitalize, will be calculated for each participating ED.
ETHICAL CONSIDERATIONS	The protocol will be submitted to the ethics committees of each center.
INFORMED CONSENT	The study will be conducted with the waiver of participants' data processing consent, following the EU legislation. The institutional website of the participating centers will inform users about the center's participation in the eCREAM project.
SPONSORSHIP AND COORDINATION	The study is sponsored by the IRFMN, Milan, a not-for-profit organization. The Fenice coordinating center at the IRFMN, will coordinate the study.
FUNDING	The study is supported by the European Commission (Grant Agreement no. 101057726), UKRI (UK Research and Innovation), and SERI (Swiss State Secretariat for Education, Research and Innovation).

1. **INTRODUCTION**

1.1 Background

The literature provides several studies describing wide variations in hospital admission rates from the emergency department (ED)[1–3] at the regional, hospital and physician levels. This variability is such that it cannot be explained entirely by differences in the department's case mixes [4,5]. Among the many factors influencing this variability, inappropriate hospitalization is one of the most worrisome. It is estimated that the proportion of this phenomenon varies between 19% and 40% in Europe [6]. The consequence of such variability can be significant, as a high propensity to hospitalize patients translates into ED and hospital overcrowding, with negative implications for patient outcomes [7]. Considering that, for example, in Italy, there are about 24,000,000 passages through the ED per year, leading to approximately 3,500,000 hospitalizations [8], it is easy to see that reducing the number of inappropriate hospitalizations even by a small amount can have a significant effect in terms of pressure on hospital departments.

Furthermore, admitting a patient with no real need not only negatively impacts the crowding of the ED and the hospital but also inevitably induces unnecessary tests and treatments [9]. This phenomenon exposes patients to the risk of even serious adverse events, avoidable clinical errors [10], unmotivated emotional and physical distress, and a major economic burden to them and to society [11]. Accordingly, the rate of ED hospitalization is considered a primary performance indicator of these departments, and there is continuous pressure for its reduction. There is, however, the flip side of the coin. An overly optimistic assessment of the patient's condition in the ED and subsequent improper discharge can also have serious health consequences and trigger lengthy litigations. Hence, improving the appropriateness of this decision is of paramount public interest to protect individual patients, on the one hand, and to reduce the massive waste of resources that characterizes today's system on the other.

Inducing improvements in complex decision-making processes within organizations that are themselves complex is a challenge that has generated vast literature in various scientific disciplines, from psychology to sociology to educational science [12]. Whatever the model of reference adopted, the first step is invariably to arouse in system actors a widespread sense of the need for change. From this perspective, peer-to-peer comparison has long been considered one of the most effective approaches to achieve this goal [13,14].

In our context, peer-to-peer comparison means center-to-center comparison, which requires adjusting for possible differences among centers to be fair and convincing. The first step to reach this goal is to develop a predictive model that accurately estimates each patient's probability of being admitted, starting from clinical conditions and boundary variables. Such a model would make it possible to calculate, for each ED, the expected hospitalization rate; that is, the hospitalization rate that would have been observed if the ED had behaved like the average of the EDs that provided the data to build the model itself. Comparing the observed hospitalization rate in the single ED with the expected rate derived from the model provides a rigorous method of comparing the department with the average performance, taking into account the characteristics of the patients treated and the conditions under which the ED operated. In other words, the predictive model represents the benchmark against which each ED is evaluated.

In this framework, choosing the predictors to use in the model becomes critical. If relevant factors are omitted and are not balanced across the EDs, the predictive model may estimate a similar expected number of hospitalizations for centers with different case mixes, introducing a significant bias in the comparison of centers.

Previous studies have fed such models with the patients' characteristics available in administrative databases, primarily age, sex, race/ethnicity, mode of arrival at the ED, and arrival day/time [15]. Other studies have leveraged

the information contained in parallel databases, such as historical insurance claims, to determine comorbidities[1]. However, the limited amount of structured information and the lack, or oversimplification, of critical factors describing signs, symptoms, and disease acuity in the available databases have hindered the development of reliable benchmarking models [4]. It should be noted that, while the decision to admit a patient is straightforward for patients in serious conditions and relatively few variables are sufficient to predict it, in most cases the decision is not so clear, and physicians must carefully weigh several factors, including those related to clinical and social well-being. Predictive models must include these factors to produce a valuable and convincing benchmark. The vast number of patients visiting an ED and the staff shortage that often afflicts these departments, however, make ad hoc data collection almost unachievable in emergency medicine. The only way to fill the gap between the need for research and the availability of high-quality data is to extract data directly from the EDs' electronic health records (EHRs), avoiding dedicated data collection.

1.2 The eCREAM project

eCREAM (enabling Clinical Research in Emergency and Acute-care Medicine) is a European project coordinated by the Laboratory of Clinical Epidemiology at the Istituto di Ricerche Farmacologiche Mario Negri IRCCS (IRFMN). It involves 11 partners in 8 countries (France, Greece, Italy, Poland, Slovakia, Slovenia, Switzerland, and the United Kingdom).

eCREAM has three main aims: 1) to develop new technical solutions to extract reliable clinical information from structured and unstructured data contained in different electronic patient files, with the use of Natural Language Processing (NLP) technology (see paragraph 1.3), to interpret the unstructured data and extract essential information for analysis; 2) to pilot the exploitation of the databases created with the use of the NLP technology in two relevant use cases: the assessment of ED propensity to hospitalize a patient (use case 1), and the development of a dashboard to be used by citizens and policymakers to improve the quality of care in ED (use case 2); 3) to FAIRify (i.e., make data Findable, Accessible, Interoperable, and Re-usable) the established databases for clinicians, researchers, health policymakers and citizens, respecting the European and national legislations.

eCREAM has been financed by the European Commission under the *Horizon Europe* program (Grant Agreement no. 101057726), UKRI (UK Research and Innovation), and SERI (Swiss State Secretariat for Education, Research and Innovation).

1.3 The eCREAM Language Model

One of the main aims of eCREAM is to develop and validate a language model (called *eCREAM_LM*) for the six languages of the project (English, Greek, Italian, Polish, Slovakian, and Slovenian), able to interpret the content of ED EHRs and to directly and automatically extract information necessary for research purposes. *eCREAM_LM* is an NLP model based on deep learning architectures, developed and validated in the context of the project. This language model will extract the data identified as necessary to carry out this Use Case 1 study, omitting the collection of any identifying data present in the free text note fields.

2. **OBJECTIVES OF THE STUDY**

The general aim of this study, which refers to Use Case 1 of the eCREAM project (eCREAM-UC1), is to test the solutions for extracting structured data from different electronic patient records in a use case relevant to EDs, i.e.,

the propensity to hospitalize patients. The analysis will focus on two subgroups of patients: those presenting to the ED with dyspnea and those presenting following a transient loss of consciousness (TLoC). We will also investigate the association between the adjusted hospitalization rate of different EDs and a short-term clinical outcome (i.e., 30-day survival) to test the possibility of extracting data from administrative records.

According to this framework, the primary objectives of the study are:

1) to create two separate databases (one for each of the two subgroups considered) on all patients who presented to the participating EDs over a defined period, containing the information considered important to study both the propensity to hospitalize these patients and their 30-day mortality;
2) to develop two multivariable models that predict the probability that patients presenting to the ED with dyspnea (first model) or after a TLoC (second model) will be admitted to the hospital;
3) To provide the participating EDs with an adjusted comparison of the hospitalization rates for the patients with selected symptoms, to improve the quality of care.

Secondary objective:

1) to assess the association of the adjusted admission rate with 30-day survival.

3. **STUDY DESIGN**

Observational, multicenter, retrospective study.

4. **PARTICIPATING CENTERS AND STUDY POPULATION**

4.1 Participating centers

The EDs adhering to the eCREAM project will participate in the study, with the exclusion of centers in Greece, as they are currently not using an EHR. Overall, 30 EDs will be included: 16 from Italy, 4 from Poland, 3 each from Slovakia, Slovenia and UK, and 1 from Switzerland. The complete list of participating centers is reported in Annex 1. The centers will not receive any incentive for participating in the study, but expenses incurred for participation will be covered by project funds.

4.2 Study population

All patients who arrived at the participating EDs between January 2021 and December 2023 will be eligible for the restricted data collection (see section 5.2.). This is a minimum dataset that will allow the estimation of the level of crowding in the ED (distinguished by priority code), the average boarding time of patients to be hospitalized, the flow of incoming patients, and other conditions. These elements are among the factors that influence the decision to admit or discharge a patient (the subject of the study) and can only be derived from data collected on all patients arriving at the ED. Patients referred to a specialist outside the ED (e.g., pediatrician, orthopedic surgeon, ophthalmologist) who, consequently, do not contribute to ED crowding will be excluded.

Two subgroups of patients will be eligible for the extended data collection (see section 5.2.):

- Adult patients who presented to the ED with dyspnea. These patients will be automatically identified by analyzing the triage section of the EHRs. In particular, both the field dedicated to the main reason for arrival at the ED and the free text notes taken by the triagist will be considered.
- Adult patients who presented to the ED following TLoC. To reduce the complexity of such a vast group of

patients, we will limit the analysis to those who experienced TLoC due to epilepsy or syncope. These patients will be identified by analyzing the triage section and the final ED diagnosis. Regarding the triage section, both the field dedicated to the reasons for arrival to the ED and the free text notes taken by the triagist will be considered. The final diagnosis section will be used to restrict the study to patients with epilepsy or syncope.

5. **STUDY PLAN AND METHODS**

5.1 Study duration

The eCREAM-UC1 will last 24 months: the first 12 will be used to install the eCREAM IT platform in the various participating EDs and to retrieve the required clinical and administrative information, checking its quality and making any necessary adjustments; the second 12 months will be devoted to data analysis, production of research reports, and dissemination of results.

5.2 Data collection

Three sets of information influence the decision to admit or discharge a patient with dyspnea or TLoC and, therefore, should be collected during the eCREAM-UC1.

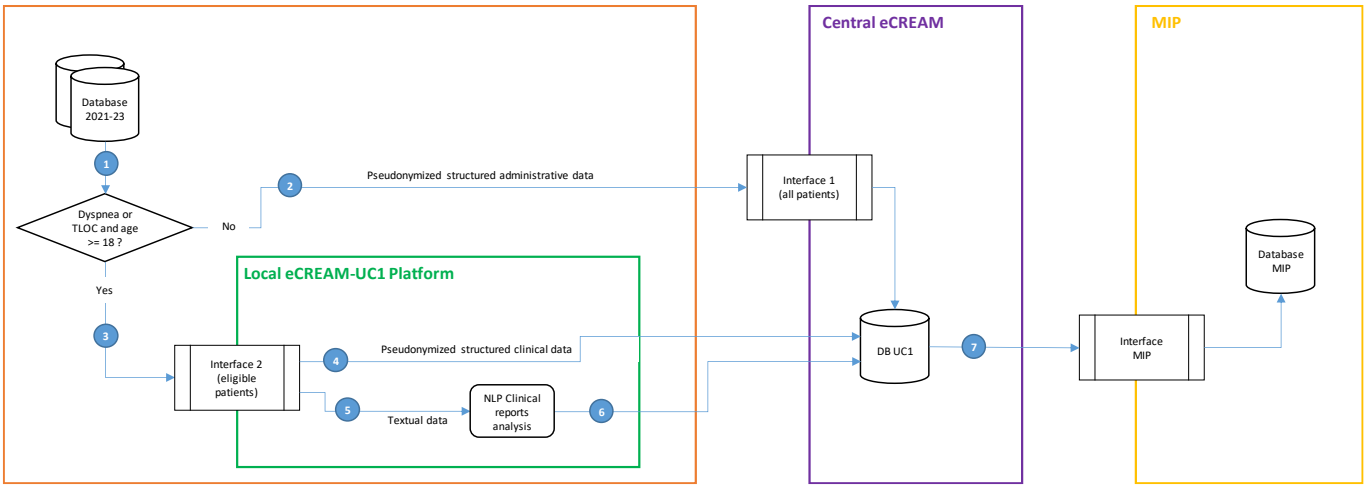
- Structural organizational data (e.g., the possibility of performing a given diagnostic test in outpatient clinics without significant delay), which will be collected at the ED level through a questionnaire to the ED staff or department head and do not include patient data. Annex 2 reports the questionnaire on structural organizational data.
- Transitory organizational data (e.g., real-time crowding level in the ED and the hospital), which will be estimated based on the restricted data collected on all patients who transit through the ED. In this framework, the only variables collected on all patients will be those that allow for the calculation, at any given time, of the number and type of patients in the ED, as well as for the timing of certain specific phases (restricted data collection, see Annex 3).
- Data on patients with dyspnea or TLoC at ED arrival (extended data collection). The variables needed for predicting the hospitalization of these patients were identified through a Delphi-modified method and literature review. An international panel of experts was asked to select the variables that, in the two selected cases, may affect the final choice of admission or discharge. According to the minimization principle, only the variables indicated by the panel will be collected, taking into account two separate lists for the two types of patients so as to collect as little information as possible on each patient. Since no active data collection is requested from the participating centers, as all necessary information will be obtained directly and automatically from the EHRs in use in the ED, we refer to this list of variables as the eCREAM virtual case report form (vCRF, Annex 4).

In each participating hospital, we will install the eCREAM IT platform, created by Astir S.R.L. and specifically designed to extract information from structured (e.g., lab test results) and unstructured (e.g., clinical notes) data contained in the EHRs of the ED and other patient records. The information needed to obtain transitory organizational data and data on patients with dyspnea and TLoC will be obtained automatically through this platform. For this purpose, the platform will be equipped with the eCREAM NLP system developed by Fondazione Bruno Kessler (FBK)

and Orobix Life S.R.L. (Orobix) to identify, in the clinical notes, the variables listed in the vCRF. The server farm used to provide the architecture will be certified according to the ISO 27018 protocol, a standard specifically developed for cloud computing service providers to ensure compliance with the privacy principles and regulations under the GDPR.

5.3 Data processing

The processing of data collected in the context of eCREAM-UC1 has been planned with the specific aim of protecting, to the highest possible level, the privacy of the patients involved. The figure reproduced below presents a simplified representation of the processing that will be carried out. Further details can be found in Annex 5.



The first step will be for the hospital information system managers to identify patients eligible for extended data collection (i.e., those who accessed the ED for dyspnea or loss of consciousness) and those who are not eligible. For non-eligible patients, pseudonymized administrative information will be transferred (second step) to the study's central server through a specific interface (Interface 1 in the diagram). These data will serve to calculate the presence, at any given time, of patients in the ED and the timing of certain specific phases of the taking on of a patient.

In the third step, all data available on eligible patients will be passed to the Local eCREAM-UC1 Platform, which will perform two tasks. First, it will retrieve the information collected in the study's data collection form (vCRF, see Annex 4) that is already structured in the available sources, such as laboratory test results, and transmit it to the Central eCREAM Server (step 4). Second, it will send the available textual information to the NLP system embedded in the Local Platform to transform unstructured information into the structured clinical data provided by the vCRF (step 5). The data thus obtained will be transferred to the central eCREAM server (step 6), where it will be merged with the other two databases received to create the UC1 study database. An additional step (step 7) will consist of transmitting the database, after appropriate data curation, to the Medical Informatics Platform (MIP, see paragraph 8.5, step 7).

For more details on the data processing procedure, see Annex 5.

By adopting this data processing plan, only data necessary to pursue the study objectives will be transmitted from the participating centers to the study coordination center.

Before data analysis begins, the coordinating center will assess the internal consistency of the information collected (see Section 9).

5.4 Data storage

Since one of the main commitments of eCREAM is to make the data FAIR (Findable, Accessible, Interoperable and Reusable) to increase the value of scientific research, the data collected in eCREAM-UC1 will be centrally stored in the eCREAM project's central server and the Medical Informatics Platform (MIP, see paragraph 8.5) for 20 years from the study closure date. The eCREAM project's central server is located in Milan, Italy, and the Medical Informatics Platform is installed on the EBRAINS server located at the Centro Svizzero di Calcolo Scientifico (CSCS) in Lugano, Switzerland. At that point, all data collected for this study will be permanently deleted. Should the data be considered of particular interest for other scientific purposes, specific authorization will be requested from the competent ethical authorities to extend the duration of the storage.

5.5 Data protection

The processing of data collected in the context of eCREAM-UC1 has been planned with the specific aim of protecting, to the highest possible level, the privacy of the patients involved. Annex 5 provides details on data processing and protection.

5.6 Statistical analysis

Primary objective 1 (extraction of datasets). This objective does not require any statistical analysis.

Primary objective 2 (development of predictive models). Due to substantial between-center differences in patient case mix, staffing conditions, and hospital and regional characteristics, comparison of hospitalization rates must use appropriate statistical methodology to be fair. A multivariable model will be used to estimate the probability of hospitalization based on patient-specific factors (e.g., medical conditions), transitory-specific factors (e.g., ED crowding), hospital-specific factors (e.g., availability of medical resources), and societal-specific factors (e.g., presence of healthcare services). The type of model to be used will need to address two peculiarities of the data. First, ED patients do not all undergo the same exams, tests or specialized visits. When a test is not performed, its result is inherently missing and, in general, cannot be considered as physiological. In particular, this absence (missingness) is informative, because physicians decide on the administration of diagnostic tests based on the characteristics of patients. Thus, for tests that are relevant to the decision to hospitalize a patient, the adopted model must handle such informative missingness by considering, both, whether the test was performed and, if that is the case, its result. Traditional regression models, such as logistic regression, are not appropriate for this task, because they require complete data for all of the predictors. The second peculiarity of our data source is that several factors are expected to heterogeneously affect the decision to hospitalize in different subgroups of patients. For example, in the context of TLoC, younger age may increase the likelihood of hospitalization in case of epilepsy (since the first episodes require in-hospital observation) and decrease it for syncope. The adopted model must be flexible enough to capture such heterogeneity. Again, traditional regression models are not suitable for this task, as heterogeneity can only be modeled with prespecified interactions among factors. This is impossible for this application, because the weight of multiple factors potentially depends on several other characteristics of the patients. In this context, decision trees represent a broad family of statistical models that properly address these two characteristics of the

data. Specifically, on the one hand, these models efficiently handle missing data through the Missingness Incorporated in Attributes (MIA) procedure, which has been shown to outperform solutions implemented for other families of models in the presence of informative missingness [16,17]. On the other hand, the nonparametric nature of decision trees makes them very flexible and capable of capturing heterogeneous effects. We will explore the use of different models from this family, including Classification and Regression Trees (CARTs), Boosted Trees, Random Forests and Bayesian Additive Regression Trees (BARTs). We will select the specific algorithm with the best performance, which will be evaluated in terms of discrimination (with the area under the ROC curve) and calibration (using the Calibration belt [18,19]). In particular, the development of a model that achieves acceptable calibration (nonsignificant test associated with the Calibration belt) and adequate discrimination (area under the ROC curve>0.8), i.e., good performance estimating the probability of patients being hospitalized, will support the reliability of the information extracted from the EHR of the participating centers for the purposes of this research project.

Primary objective 3 (adjusted comparison of hospitalization rates). The multivariable model will provide the probability each patient had of being hospitalized, conditional to the relevant predictors. We will estimate the expected center-specific hospitalization rate by summing these probabilities over all patients visiting a single ED. The ratio between observed and expected rates, which will be referred to as standardized hospitalization rate (SHR), which represents an adjusted indicator to measure the propensity of the ED to hospitalize patients. The SHR will be provided with the corresponding 95% confidence interval based on the binomial distribution [20]. This, along with other specific indicators, will be the object of a reporting activity to the participating centers, with the aim of feeding them back a comprehensive self-assessment tool (see par. 5.6).

Secondary objective (association with patients' mortality). To assess the association of the adjusted admission rate with 30-day survival, we will use a multivariable logistic regression model. We will consider the 30-day survival as the model's response and include, as predictors, the SHR estimated for primary objective 3 and other prognostic relevant factors. The coefficient of the SHR in the model will inform on the association between the ED-specific propensity to hospitalize patients and the patients' outcomes, after adjusting for patient-specific prognostic factors.

5.7 Sample size

The sample size must be calculated separately for the study objectives requiring statistical analyses.

Primary objective 2. Following the recommendation of 10 events and non-events per variable for binary outcome models [21], at least 200 hospitalized and 200 discharged patients from the ED are needed to develop a model with 20 predictors, a number about three times higher than that of the models recently published in the literature [1–4,15,22–26]. Assuming hospitalization rates of 20% and 50% for dyspnea and TLoC, at least 400 and 1,000 patients are needed, respectively.

Primary objective 3. With a type-I error of 5% and a power of 90%, to be able to detect as significant an SHR of 1.2 (i.e., an observed hospitalization rate 20% higher than expected), the study will need at least 577 and 1,442 patients with dyspnea and TLoC respectively, for each ED.

Secondary objective. Based on prior studies [27,28], we expect a 30-day mortality of 5% and 1.6% in patients presenting to the ED for dyspnea and TLoC respectively. Using the rule of 10 events per variable, we will need a total of 12,500 and 4,000 patients to develop a model including 20 predictors.

In summary, to address all the objectives of the study, the most stringent requirement regards primary objective 3, which requires data collection on about 600 and 1,500 patients presenting to the ED for dyspnea and loss of

consciousness, respectively, from each of the 30 participating centers. In a previous analysis that involved a mid-size (about 60,000 patients/year) Italian ED (Maggiore Policlinico Hospital, Milan) over the years 2017-2019, the proportion of patients with dyspnea and TLoC was 3.5% and 2.5%, respectively, which correspond to about 2,100 and 1,500 patients/year. Because we will also include smaller EDs (even with about 30,000 patients/year), and to be conservative, eCREAM-UC1 plans to retrospectively analyze eligible patients visiting the participating EDs over three years. This means that we will recruit at least 3,150 patients with dyspnea and 2,250 patients with TLoC in each participating center. This sample size will be more than enough to develop the predictive models, compute the ED-specific indicators on a meaningful group of patients, and evaluate the association between propensity to hospitalization and 30-day survival. Should any participating centers not enroll enough patients in either of the two groups, we plan to extend the retrospective data collection for an appropriate period of time to achieve the desired target.

5.8 Reporting indicators of propensity to hospitalization to the participating centers

Each ED will receive a personalized report with the results of the eCREAM-UC1. The report will provide a description of the eligible patients and the SHR, the primary indicator to evaluate the propensity to hospitalization. In addition, we will provide the participating centers with two further indicators, offering additional insights into the decision to hospitalize patients.

Borrowing from the variable life-adjusted display (VLAD) [29], we will develop the variable hospitalization-adjusted display (VHAD). This shows each ED's propensity to hospitalize (y-axis) against time (x-axis). When the plot rises, the ED hospitalized more patients than expected, when it declines, fewer patients than expected were hospitalized. Such a plot allows EDs to study time-related modifications of the propensity to hospitalization.

The second indicator is the Calibration belt [18,19] for hospitalization. The Calibration belt, developed by the coordinating center, represents the confidence band concerning the relationship between the observed and expected rates of an event of interest, in our case, patient hospitalization. A statistically significant deviation from the hypothesis of perfect calibration, i.e., when the single ED behaves differently from the average performance, occurs when the 95% confidence boundaries of the belt do not include the bisector.

The availability of these indicators, which characterize the propensity of patients to be hospitalized in general, over time, and according to the patient's likelihood of being hospitalized, is a powerful stimulus for participating EDs to conduct a critical appraisal of clinical practice aimed at improving healthcare quality.

6. **ADVERSE EVENTS**

eCREAM-UC1 is a retrospective observational study and monitoring of adverse events is therefore not necessary.

7. **STUDY MONITORING**

Since this is a retrospective study, there will be no on-site monitoring. The coordinating center will oversee data collection centrally to ensure the highest quality of data.

8. **ETHICAL CONSIDERATIONS**

8.1 The legal basis for data processing

eCREAM-UC1 will be conducted following the principles set out in the Helsinki Declaration, while waiving the data processing consent of each participant. Data processing consent is a fundamental protection for research participants and the preferred legal basis to process personal data lawfully. However, due to the retrospective nature of this study and in light of the large number of patients involved, acquiring consent from the participants would involve a disproportionate effort. Furthermore, a vast proportion of patients would end up being impossible to contact, significantly reducing the number of patients included and thus introducing both quantitative and qualitative biases that would preclude the fulfillment of the eCREAM-UC1 objectives. Indeed, the construction of valid and reliable predictive models relies on the availability of data on a large and truly representative patient population.

EU Regulation 2016/679 Article 9, paragraph 2, letter j provides that the data subject's consent is not required when the processing is necessary, among other conditions, for scientific research purposes, in accordance with Article 89(1), based on Union or national law, provided that it is proportionate to the purpose pursued, respects the essence of the right to data protection, and provides for appropriate and specific measures to protect the fundamental rights and interests of the data subject. It is noteworthy that in establishing the new Horizon Europe framework program, the EU emphasized the need to carry out joint and coordinated actions to address the crisis and make Europe a knowledge-based economy. Projects funded under the Horizon Europe Program are therefore to be considered in the same manner as those based on laws of the Union. Paragraph 1 of Article 89, chapter IX, which is recalled here, states, "Processing for archiving purposes in the public interest, scientific or historical research or statistical purposes shall be subject to appropriate safeguards for the rights and freedoms of the data subject, in accordance with this Regulation. Such safeguards shall ensure that technical and organizational measures are in place, in particular to ensure compliance with the principle of data minimization. Such measures may include pseudonymization, if the purposes in question can be achieved in this manner. Where they can be achieved by further processing that does not allow, or no longer allows, the data subject to be identified, those purposes must be achieved in this manner."

Unfortunately, data cannot be anonymized in this study for two main reasons. First, in order to ensure the highest level of data quality, the coordinating center can request clarifications from participating centers in case of missing, conflicting, implausible, or insufficiently clear information. To reply to the queries, participating centers may need to access additional (hospital) information and may therefore need to identify the patients who are the subject of the clarification requests. Second, anonymizing patient-level data means applying techniques that make subjects less identifiable, such as data generalization, swapping, and perturbation. The downside of this process is that it affects the ability to make correct inferences and, thus, the usefulness of the data. In our study we are collecting data starting from what physicians and nurses decided to write in the EHR, which is, by definition, non-systematic. We expect many missing values and variables defined in heterogeneous ways. This will result in our having to deal with a higher-than-usual level of noise. Introducing an additional source of artificial noise would jeopardize our ability to derive reliable knowledge from these data and would risk undermining the effort made to collect it. Consequently, the database will be appropriately pseudonymized before it is transferred to the coordinating center.

Measures to protect the rights and welfare of the subjects will be implemented, including: 1) masking or deleting any personal data (e.g., date of birth, exact time of day); 2) consultation and approval of the study protocol by Ethics Committees; 3) consultation and approval of the legal basis for data collection and processing by the National Data

Protection Authority, where appropriate; 4) informing people who visited participating EDs during the study period about the project through communication on the institutional websites (see Annex 6); 5) public disclosure of the results following the completion of the study. Moreover, the principle of minimization is strictly ensured (see paragraph 5.3), and a rigorous database security system will be in place (see Annex 5).

Finally, as EU Regulation 2016/679 provides that Member States may maintain or introduce more specific provisions to ensure lawful and fair processing of genetic data, biometric data or data concerning health, we must comply with all of these possible additional provisions, as well as with the privacy protection provisions in place in the consortium states that are not members of the European Union (UK and Switzerland). Each participating country will provide details on the specific provisions that apply to that country. An analysis of these provisions for Italy is presented below.

8.1.1 Italy

Articles 110 and 110bis of Legislative Decree No. 196/2003 (Italian Personal Data Protection Code), which address the issue of medical, biomedical and epidemiological research, allow for exceptions to the legal basis of data processing consent.

Paragraph 1 of Article 110, which recalls Article 9, paragraph 2, letter j of EU Regulation 2016/679, stipulates that research projects carried out on legislative or regulatory provisions or EU law, for which the data subject's consent to data processing is not necessary, also include those approved under the biomedical or health research program referred to in Article 12-bis of Legislative Decree No. 502 of December 30, 1992. By analogy, research projects approved and funded by the European Commission, such as the eCREAM project, should also fall under this instance. In addition, the same paragraph 1 of Article 110, as well as paragraph 1 of Article 110bis, states that consent is not necessary when, due to special reasons, informing the persons concerned proves impossible or involves a disproportionate effort, or risks making it impossible or seriously undermining the achievement of the purposes of the research. Both these conditions hold for the eCREAM-UC1 study.

8.2 Insurance

Considering the study design and observational approach, no study-specific insurance coverage is required for this study.

8.3 Ethics Committee

This study protocol will be submitted to all ethics committees of participating centers, according to the national legislation for observational studies.

8.4 Publication of Data

The Scientific Committee will decide on publications. The authors to be reported on the front page will be selected based on their specific contributions to the project. All manuscripts will include an appropriate acknowledgment section, mentioning all physicians who contributed to the study and all supporting agencies, making explicit reference to the European grant that enabled the project to be carried out. Research results will be published irrespective of the findings.

8.5 Data Sharing – the MIP

One of eCREAM's goals is to maximize the exploitation of the collected data for secondary research or monitoring activities. This goal falls within the FAIR guiding principles (to enhance the Findability, Accessibility, Interoperability and Reusability of digital resources such as data) that the project follows. eCREAM will therefore develop a strategy for assembling the databases created to address the two use cases to permit users outside the consortium to use them. To this end, eCREAM will join the MIP (Medical Informatics Platform), developed in the Human Brain Project (HBP), to federate clinical data. The MIP is an open-source, GDPR-compliant, privacy-aware platform, enabling remote and federated analyses from datasets physically distributed in various hospitals, research centers, and biobanks, without moving the data outside their original storage site to a central repository. Patient identification data will be deleted from the databases before these are uploaded to the MIP platform, and no pseudo-identifier will be available.

Three different MIP instances will be set up. The public MIP, located on the EBRAINS (https://ebrains.eu/) research infrastructure, will include a subset of the eCREAM database (corresponding to the restricted data collection) made publicly available to a broader community, including citizens. The eCREAM MIP will be installed on a dedicated secured server on the EBRAINS research infrastructure and will contain the central eCREAM database. Access will be restricted to a defined set of accredited end-users and monitored and recorded. The Federated MIP will enable partnering organizations wishing to federate their data with the eCREAM-MIP to install other MIP instances on the EBRAINS research infrastructure. The overall MIP security system will enable the precise definition of which data will be made available to each user and with which level of access, providing full control over data analyses. See https://mip.ebrains.eu/ for more details on the MIP.

9. **QUALITY ASSURANCE**

Data will be reviewed centrally by the coordinating center to look for inconsistencies. Specifically, two types of problems will be considered: inconsistency or implausibility per se (e.g., incorrect date) and inconsistency or implausibility relative to other variables (e.g., respiratory failure without ventilation). Queries will be sent to the participating EDs, asking to solve all doubts raised.

10. **SPONSORSHIP, STUDY COORDINATION, AND FUNDING**

The study is sponsored by Istituto di Ricerche Farmacologiche Mario Negri IRCCS (IRFMN), Milan, a not-for-profit organization. The Fenice coordinating center at the IRFMN, Villa Camozzi, Via G.B. Camozzi 3, 24020 Ranica (Bergamo), Italy, will coordinate the study.

The study is supported by the European Commission (grant Call&Topic: HORIZON-HLTH-2021-TOOL-06-03. Type of action: HORIZON Research and Innovation Actions Project number: 101057726), UKRI (UK Research and Innovation), and SERI (Swiss State Secretariat for Education, Research and Innovation).

11. **ROLES OF RESPONSIBILITY**

The Istituto di Ricerche Farmacologiche Mario Negri IRCCS (IRFMN) is responsible for overseeing the activities requested to ensure that the study will be conducted in compliance with the protocol, applicable regulatory requirements and international guidelines. The principal investigator and the scientific committee will have scientific

and operational responsibility. The IRFMN will be the data controller of the central eCREAM system.

Astir S.R.L. is responsible for installing the Local eCREAM Platform within the information systems of the participating centers. It will have access to the data for maintenance purposes and will act as data processor for the single clinical centers. The platform will receive the data from the centers and transfer it to the study's central server. Astir S.R.L. will also act as data processor for the IRFMN since they will be responsible for the central eCREAM software infrastructure and will have access to the data for technical support and maintenance.

Each country coordinator/national study contact will be responsible for obtaining ethical, regulatory, and legal authorizations in compliance with the European and local provisions, including the GDPR and national data protection regulations.

The individual EDs participating in the project will be data controllers of their own EHR data.

The Centre Hospitalier Universitaire Vaudois (CHUV) is responsible for integrating the eCREAM database within the Medical Informatics Platform to make the project's data accessible outside the consortium and will act as data processor for the IRFMN concerning the data on the MIP.

AWS (Amazon Work Services) will provide the Cloud service and will act as sub-processor for Astir S.R.L.

FBK and Orobix will act as co-processors for Astir, since they will have access to the data if maintenance of the NLP system they developed is necessary.

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Propensity to hospitalize patients from the ED in European centers

ANNEX 1

List of participating centers and relative PIs

Version 2.0

Ranica, July 9, 2025

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eCREAM Use Case Study 1

Propensity to hospitalize patients from the ED in European centers

An observational retrospective quality-of-care study

ANNEX 2

Structural data questionnaire

Version 5.0, 15 April 2024

Ranica, Italy

clinicaltrials.gov n: NCT06354764

eCREAM Coordinating Center
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STRUCTURAL DATA QUESTIONNAIRE - ED

The aim of this questionnaire is to collect structural data to have a complete overview of your ED's organization. This data collection will be useful to compare different hospitals involved in the eCREAM project.

It is composed of 5 different sections that you have to keep in mind while filling out the form (in the web version, it will be easy to follow this schema):

1. *General data*
2. *Triage*
3. *Short stay/observation unit*
4. *General Emergency Department*
5. *Emergency Medicine Ward*

Please, refer to the data for 2022 (the whole 12 months of the year).

---

1. GENERAL DATA

General characteristics

Catchment area (consider the 12 months preceding the filling date)

Number of potential patients: _____

Are you a designated hub center for one or more diseases?

- o Yes
- o No

If yes, you are a designated hub center for:

- ☐ Polytrauma
- ☐ Neurosurgery
- ☐ Stroke
- ☐ STEMI
- ☐ Cardiac surgery
- ☐ Vascular surgery
- ☐ None of the above

Number of yearly visits, excluding fast-track accesses (consider the 12 months preceding the filling date)

Number: _____

Is any fast-track pathway implemented?

- o Yes
- o No

If yes, what kind of fast-track pathway is implemented in the hospital?

- ☐ Ophthalmology – number: _____
- ☐ Otolaryngology – number: _____
- ☐ Dermatological – number: _____
- ☐ Orthopaedic – number: _____
- ☐ Psychiatric – number: _____
- ☐ Gynecological – number: _____
- ☐ None of the above

Patients statistics

Is the number of patients discharged home from the ED monitored?

- Yes
- No

If yes, indicate the total: _____

Is the number of patients deceased in the ED monitored?

- Yes
- No

If yes, indicate the total: _____

Is the number of patients hospitalized from the ED monitored?

- Yes
- No

If yes, indicate the total: _____

Is the number of patients leaving without being seen (i.e., before the start of the visit) monitored?

- Yes
- No

If yes, indicate the total: _____

Is the number of patients leaving after the start of the visit monitored?

- Yes
- No

If yes, indicate the total: _____

---

2. TRIAGE AND POST TRIAGE

General characteristics

Is a dedicated pediatric triage implemented?

- Yes
- No

If yes, is it managed separately from the general ED?

- Yes
- No

Is a dedicated gynecological triage implemented?

- Yes
- No

If yes, is it managed separately from the general ED?

- Yes
- No

Is a dedicated obstetric triage implemented?

- Yes
- No

If yes, is it managed separately from the general ED?

- Yes
- No

Is a dedicated trauma triage implemented?

- Yes
- No

If yes, is it managed separately from the general ED?

- Yes
- No

Is a dedicated triage for infectious diseases implemented?

- Yes
- No

If yes, is it managed separately from the general ED?

- Yes
- No

Is any other specialistic triage implemented?

- Yes
- No

If yes, specify which other specialistic triage is implemented.

Text: _____

Is it managed separately from the general ED?

- Yes
- No

Spaces

Does the ED have a heated area right outside the entrance?

- Yes
- No

If yes, how many ambulances can enter this area?

Number: ____

Does the ED have a decontamination area?

- Yes
- No

Is administrative registration performed as a separate step from triage?

- Yes
- No

If yes, is it performed in a dedicated area?

- Yes
- No

When is it performed?

- 12h/day
- Always

Are there separate paths for patients walking or on stretchers?

- Yes
- No

The triage is performed:

- At a counter
- In dedicated rooms

If "in dedicated rooms" is selected, indicate the number of rooms dedicated to the triage.

Number: _____

Square meters per room

Number: _____

Is the number of air changes per hour in the triage rooms available?

- Yes
- No

If yes, number of air changes per hour:

Number: _____

Is negative pressure available in at least one of the triage rooms?

- Yes
- No

Does the ED have a dedicated area to transfer patients from stretchers?

- Yes
- No

Is there a pre-triage waiting area?

- Yes
- No

Are there dedicated spaces for the post-triage activities preceding the medical examination?

- Yes
- No

If yes, are there dedicated rooms/cubicles for the nurse-initiated treatments?

- Yes
- No

Is there a waiting area for the relatives of patients?

- Yes
- No

If yes, surface area in square meters

Number: _____

Does the room have a dedicated staff?

- Yes
- No

Are there screens for weight management?

- Yes
- No

Are there dedicated toilets for waiting patients?

- Yes
- No

Is there a video surveillance system in the triage area?

- Yes
- No

Is there a security service?

- Yes
- No

Resources and equipment

Is the triage system computer-based?

- Yes
- No

Indicate the number of computer workstations dedicated to the triage:

Number: _____

Are electrocardiographs or other equipment to perform ECGs available?

- Yes
- No

If yes, how many?

Number: _____

Are multi-parameter patient monitors available?

- Yes
- No

If yes, how many?

Number: _____

Are backboard/mattress splints for spinal immobilization available?

- Yes
- No

Point of care devices:

- ☐ Blood gas analyzer
- ☐ Troponin
- ☐ Coagulation
- ☐ Ultrasound
- ☐ Blood glucose test (finger prick)
- ☐ None

Work organization

Are standardized triage protocols in place?

- o Yes
- o No

How many levels does the triaging system use?

Number: _____

Are there any patient identification systems (e.g., wristbands) in place?

- o Yes
- o No

Are there any identification systems in place for patients' relatives/caregivers?

- o Yes
- o No

The triage is organized as:

- o Single-step triage
- o Two-step triage

Is there any nurse-initiated treatment protocol in place?

- o Yes
- o No

If yes, for what conditions?

- ☐ Chest pain
- ☐ Abdominal pain
- ☐ Nonspecific pain
- ☐ Minor trauma
- ☐ Minor wound treatment/suturing
- ☐ Sepsis or infection
- ☐ Acute urine retention
- ☐ Renal colic
- ☐ Urinary tract infection
- ☐ COVID-19
- ☐ Other

If check on other, specify: _____

Is there a nurse-managed referral to outpatient care (e.g., schedule of outpatient appointments)?

- o Yes
- o No

Staff

Indicate the number of nurses dedicated to the triage activity per shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Indicate the number of doctors dedicated to the triage activity per shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Indicate the number of healthcare assistants dedicated to the triage activity per shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Indicate the number of administrative staff dedicated to the triage activity for each shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Indicate the number of the security service staff dedicated to the triage area for each shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

---

3. OBSERVATION UNIT

General characteristics

Does the ED have an Observation Unit?

- Yes
- No

If yes, how many beds are there in the unit?

Number: _____

Structure:

- Separate rooms
- Open space

Are there dedicated bathrooms/toilets for patients?

- Yes
- No

Does the unit have a dedicated staff?

- Yes
- No

If yes, indicate the number of attending physicians dedicated to the Observation Unit per shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Indicate the number of other physicians (e.g., residents) dedicated to the Observation Unit per shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Indicate the number of nurses dedicated to the Observation Unit per shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Indicate the number of healthcare assistants dedicated to the Observation Unit per shift:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Does the Observation Unit have an isolation room with negative pressure?

- Yes
- No

Is it equipped with infrared thermometers?

- Yes
- No

If yes, total number: ____

Is it equipped with a thermoscanner?

- Yes
- No

If yes, total number: _____

Is it equipped with pulse oximeters?

- Yes
- No

If yes, total number: _____

Do you have beds equipped with dedicated multi-parameter monitors?

- Yes
- No

If yes, total number: _____

Is it equipped with a blood gas analyzer?

- Yes
- No

If yes, total number: _____

Is it equipped with electrocardiographs or other equipment to perform ECGs?

- Yes
- No

If yes, total number: _____

Is it equipped with ultrasound machines?

- Yes
- No

If yes, total number: _____

Do you have transportable vital parameter monitoring systems?

- Yes
- No

If yes, total number: _____

Is the Observation Unit also used for Semi-intensive/high-dependency/intermediate-care treatments?

- Yes
- No

If yes, is it equipped with venturimeters/systems for CPAP administration?

- Yes
- No

If yes, total number: _____

Is it equipped with ventilators?

- Yes
- No

If yes, total number: _____

Is it equipped with oxygen delivery systems other than a CPAP helmet?

- Yes
- No

If yes, total number: _____

Is it equipped with CPAP helmets?

- Yes
- No

If yes, total number: _____

Is it equipped with dialysis/hemofiltration systems?

- Yes
- No

If yes, total number: _____

Is the Observation Unit used for patients awaiting hospitalization?

- Yes
- No

---

4. GENERAL EMERGENCY DEPARTMENT

Organization

The ED is organized according to:

- Medical specialty
- Priority code
- Intensity of care
- None of the above; it follows a mixed organization

How many simultaneous work areas/lines are there in the ED?

Number: _____

Does the initial nurse assessment take place in the medical examination area?

- Yes
- No

Are there physician-nurse shared protocols?

- Yes
- No

If yes, shared protocols for:

- ☐ Chest pain
- ☐ Syncope
- ☐ Major trauma
- ☐ Head trauma
- ☐ Sepsis
- ☐ Pulmonary embolism
- ☐ Femur fracture
- ☐ Stroke
- ☐ STEMI
- ☐ Other

Is any structured model of communication for medical handovers (e.g., SBAR) implemented?

- o Yes
- o No

If yes, are pre-printed forms used?

- o Yes
- o No

Is any structured model of communication for nurse handovers (e.g., SBAR) implemented?

- o Yes
- o No

If yes, are pre-printed forms used?

- o Yes
- o No

Is there a referent nurse for each shift?

- o Yes
- o No

Is there a formal protocol for the training of the nurses newly hired in the ED?

- o Yes
- o No

If yes, the training protocol is defined at:

- o Hospital level
- o Regional/National level

ED physicians autonomously manage:

- ☐ Electrical cardioversion
- ☐ Procedural sedation
- ☐ Dislocation reduction
- ☐ Thoracic drainage
- ☐ ECG reading and reporting
- ☐ Echography
- ☐ Central venous catheter (CVC) insertion
- ☐ Cardiac arrest
- ☐ Non-invasive ventilation (NIV)
- ☐ None of the above

Is there an outpatient clinic for low-priority/minor triage codes?

- o Yes
- o No

If yes, it is managed by:

- ☐ Medical ED staff on rotation
- ☐ Independent contractors with project-based contracts
- ☐ General practitioners
- ☐ None of the above

Is there a dedicated treatment area for walk-in patients, with low-to-medium complexity and high probability of home discharge, managed by physician-nurse teams (RATs)?

- o Yes
- o No

In the examination areas, which organizational model is adopted:

- Outpatient assessment, with patients entering and leaving dedicated areas for examination and reassessment
- Physicians move to the patients, who stay in dedicated cubicles/chairs, for the examination (doctor-to-patient approach)

Spaces

Surface area, in square meters, of the ED (excluding triage and Short Stay/Observation Unit):

Number: _____

Is there a relaxing room for the ED staff?

- Yes
- No

Is there a dedicated grieving room?

- Yes
- No

Is there a room dedicated to specialist consultant physicians?

- Yes
- No

Is there a room dedicated to gender-based violence?

- Yes
- No

Is there a room dedicated to communication with relatives?

- Yes
- No

Is there a storage room dedicated to the ED?

- Yes
- No

If yes, the surface area in square meters:

Number: _____

The ED is organized as:

- Open space
- Outpatient clinic
- Mixed organization

Are negative pressure rooms present in the ED?

- Yes
- No

If yes, the total number of rooms: _____

Number of seats dedicated to the examination: _____

Of them, the number of seats where oxygen therapy can be provided: _____

Of them, the number of seats with vital parameter monitors: _____

Number of stretcher stations in dedicated examination or post-examination area: _____

Of them, the number of stations where oxygen therapy can be provided: _____

Of them, the number of stations with vital parameter monitors: _____

Is there a dedicated pre-examination waiting area?

- o Yes
- o No

Is there a dedicated post-examination waiting area that is different from the pre-examination waiting area?

- o Yes
- o No

Total number of toilets for patients: _____

Total number of cubicles dedicated to doctor-to-patient method: _____

Resources and equipment

The system to request exams and receive medical reports is based on:

- ☐ Pneumatic mail
- ☐ The system is integrated into the ED EHR
- ☐ None of the above

Is there a radiology area dedicated to the ED?

- o Yes
- o No

Can blood cultures be processed in the laboratory 24/7?

- o Yes
- o No

How many computer workstations are there?

Number: _____

Of them, how many are dedicated to nurses?

Number: _____

Are there laptops in use?

- o Yes
- o No

Are there areas that are not directly overseen by ED/hospital staff?

- o Yes
- o No

If yes, are these areas equipped with video surveillance systems?

- o Yes
- o No

The software of the ED EHR has the following features:

- ☐ Monitor/show the patient stay time
- ☐ Track transfer to Short Stay Unit
- ☐ Display ED maps
- ☐ Assignment of patients to different areas/teams
- ☐ Track waiting time for hospital admission
- ☐ Generate medication administration record
- ☐ Prescribe medications with customizable schedules of administration
- ☐ Alert for prescribed medications to be administered
- ☐ Confirmation/signature by the nurse administering medications
- ☐ Allergy alerts
- ☐ Integration with parameters monitoring units
- ☐ Integration with risk scores
- ☐ Connection to the national/regional patient electronic health record
- ☐ Integration with laboratory
- ☐ Integration with radiology
- ☐ Integration with specialist consultants from other hospital departments
- ☐ None of the above

Staff

MEDICAL STAFF (cascading)

What is the medical specialty of the chief of the ED?

Text: _____

Does the ED have a fully autonomous staff (i.e., the physicians working in the ED only work in the ED)?

- o Yes
- o No

If no, the ED medical staff includes:

Attending ED physicians

- o Yes
- o No

Resident ED physicians

- o Yes
- o No

Surgeons

- o Yes
- o No

Physicians from other hospital departments on rotation

- o Yes
- o No

Physicians from other hospital departments as temporary contractors

- o Yes
- o No

Independent contractors

- o Yes
- o No

Physicians hired by private businesses that contract the service with the hospital

- Yes
- No

For each one, if yes:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

If yes to "Attending ED physicians", indicate the total number of attending physicians dedicated to clinical activity/patient care activity EXCLUSIVELY employed in ED activities:

Number: _____

Indicate the total number of attending physicians dedicated to clinical activity/patient care NOT EXCLUSIVELY employed in ED activities

Number: _____

If yes, the ED medical staff includes:

Attending ED physician

- Yes
- No

Resident ED physician

- Yes
- No

For each one, if yes:

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

If yes to "Attending PS physicians", indicate the total number of attending physicians dedicated to clinical activity/patient care activity EXCLUSIVELY employed in ED activities

Number: _____

Indicate the total number of attending physicians dedicated to clinical activity/patient care NOT EXCLUSIVELY employed in ED activities

Number: _____

NURSING STAFF (cascading)

Indicate the number of ED nurses dedicated to patient care per shift

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Indicate the total number of nurses dedicated to clinical activity/patient care EXCLUSIVELY employed in ED activities

Number: _____

Indicate the total number of nurses dedicated to clinical activity/patient care NOT EXCLUSIVELY employed in ED activities

Number: _____

OTHER PERSONNEL (cascading)

Does the ED staff include healthcare assistants?

- Yes
- No

If yes, indicate the number of healthcare assistants for each shift

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

---

5. EMERGENCY MEDICINE WARD

General characteristics

Does the hospital have an emergency medicine ward?

- Yes
- No

If yes, number of beds available: _____

Number of beds with vital parameters monitors: _____

Of them, does at least one bed have a telemetry system?

- Yes
- No

Is an electronic medical record used for patients?

- Yes
- No

Does the ward manage patients with CPAP/NIV?

- Yes
- No

Does the ward manage patients treated with amines?

- Yes
- No

Does the ward manage patients with polytraumas or organ failures?

- Yes
- No

Does the ward manage patients with acute coronary syndrome?

- Yes
- No

Does the ward manage patients with gastrointestinal hemorrhage?

- Yes
- No

Does the ward manage patients with hemodynamic instability?

- Yes
- No

Does the ward manage patients with invasive monitoring?

- Yes
- No

Is CVVH performed?

- Yes
- No

Are non-surgical polytrauma patients admitted?

- Yes
- No

Average length of stay in days (consider the 12 months preceding the filling date)

Number: _____

Is the emergency medicine ward adjacent to the ED?

- Yes
- No

Does the same staff manage the emergency medicine ward and the ED?

- Yes
- No

If no, what are the medical specialties of the medical staff managing the ward?

Text: _____

STRUCTURAL DATA QUESTIONNAIRE – HOSPITAL

Attention: This form must be filled out with reference to your own hospital and not to the organization to which the hospital belongs, and it must be updated any time changes occur.

---

1. ORGANIZATION

STRUCTURE AND ORGANISATION OF THE HOSPITAL

Functioning hospital beds usable for direct admission from the ED

Number: ____

Does the figure of bed manager exist?

- Yes
- No

If yes:

He/she is a:

- Nurse
- Doctor
- Administrative employee

Who is in charge of him/her?

- ED
- Hospital administration services
- Other

When is he/she active?

	Weekdays	Sunday / Holidays
Morning		
Afternoon		
Night		

Concerning the beds that are available for hospitalization from the ED, how many hospitals are they distributed in?

Number: ____

If > 1:

Is there a dedicated transport service between the different hospitals for patients with time-dependent diseases?

- Yes
- No

Is there a dedicated transport service for ordinary admissions/consultations between the hospitals?

- Yes
- No

Is there a priority for transfers from the ED?

- Yes
- No

Logistics of the hospital of the ED:

- Pavillons
- Monoblock

If "pavillons":

Is there a dedicated transport service for patients between the pavilions?

- Yes
- No

Helipad in the hospital of the ED:

- Present
- Absent

If "present":

Possibility of night flights for helicopters arriving to the hospital?

- Yes
- No

---

2. SPECIALTIES

SPECIALITIES PRESENT IN THE HOSPITAL

Medical area

Which independent departments are available in the hospital?

- ☐ Internal medicine
- ☐ Emergency medicine
- ☐ Intensive Care Unit
- ☐ Cardiology
- ☐ Neurology
- ☐ Psychiatry
- ☐ Pneumology
- ☐ Nephrology
- ☐ Infectious diseases
- ☐ Gastroenterology
- ☐ Rheumatology
- ☐ Oncology
- ☐ Haematology
- ☐ Paediatrics
- ☐ Rehabiltation
- ☐ Subacute care
- ☐ Hospice
- ☐ None of the above

For each check:

It is located:

- In dedicated department
- In a polyspecialistic area

If "dedicated departments":

Total beds

Number: ____

Specialist surgeries

Which independent surgery wards are available in the hospital?

- ☐ General surgery
- ☐ Emergency surgery
- ☐ Neurosurgery
- ☐ Polytrauma surgery
- ☐ Thoracic surgery
- ☐ Vascular surgery
- ☐ Orthopaedics
- ☐ Cardiosurgery
- ☐ Otolaryngology
- ☐ Urology
- ☐ Maxillofacial surgery
- ☐ Transplant surgery
- ☐ Gynecology
- ☐ Obstetrics
- ☐ Paediatric surgery
- ☐ None of the above

For each check:

- Dedicated department
- Beds in a poly specialistic area
- Procedures only

If "dedicated department":

Total beds:

Number: _____

Intensive care units

Which intensive care units are present in the hospital?

- ☐ General
- ☐ Medical
- ☐ General surgical
- ☐ Neurological
- ☐ Cardiological
- ☐ Cardiosurgical
- ☐ Burns
- ☐ Post-transplantation
- ☐ Paediatric
- ☐ Neonatal
- ☐ Other intensive care units

Specify: _____

- ☐ None of the above

For each check:

Number of units: _____

Total number of beds: _____

Of them, how many have the possibility of isolation?

High dependency units/semintensive care units

Which semintensive care units are available in the hospital?

- ☐ General
- ☐ General surgical
- ☐ Cardiological
- ☐ Neurological (stroke unit)
- ☐ Respiratory
- ☐ Other semintensive care units
  Specify: _____
- ☐ None of the above

For each check:

Number of units: _____

Total number of beds: _____

Of them, how many have the possibility of isolation?

---

3. SERVICES

SERVICES AVAILABLE IN THE HOSPITAL WHERE THE ED IS LOCATED

Radiology

- ☐ Conventional radiological reporting
  If checked:
  Availability:
  - Available H24 (also with telereport)
  - Available H12
- ☐ CT body
- ☐ MRI body
- ☐ CT Neuro
- ☐ MRI Neuro
- ☐ Neuroradiological reporting
- ☐ Interventional neuroradiology
- ☐ Interventional radiology
- ☐ None of the above

For each check (excluding "Conventional radiological reporting"):

Availability:

- Available H24 (also on call)
- Only available for certain hours of the day (also on call)

General LAB

Is the laboratory available in the hospital?

- Yes
- No

If yes:

The service is

- Available H24 (also on call)
- Only available at certain hours of the day (also on call)

Is there a dedicated working line for the ED?

- Yes
- No

If yes:

Reporting of the ED-dedicated line:

- H24
- H12
- Less than H12

Microbiology LAB

Is the laboratory available in the hospital?

- Yes
- No

If yes:

The service is

- Available H24 (also on call)
- Only available at certain hours of the day (also on call)

Can cultures be processed H24?

- Yes
- No

If yes:

Is it possible to perform rapid tests for the identification of micro-organisms (e.g. MALDI TOF)?

- Yes
- No

Other services

☐ Interventional haemodynamics

If checked:

Availability:

- Available H24 (also on call)
- H12 with on-call
- H12 without on-call
- Less than H12

☐ Digestive endoscopy

☐ Bronchoscopy

☐ Hyperbaric chamber

☐ Blood transfusion +center

☐ None of the above

For each check (excluded "Interventional haemodynamics"):

Availability:

- Available H24 (also on call)
- Only available for certain hour of the day (aalso on call)

---

4. TRAUMA MODEL

TRAUMA ORGANISATIONAL MODEL

Are the operating room and radiodiagnostics dedicated to trauma adjacent to the ED?

- Yes
- No

Is there a trauma team in the hospital?

- o Available H24 (also on call)
- o Only available on certain hours of the day (also on call)

If yes:

Which specialists are included in the trauma team?

- ☐ Surgeon
- ☐ Orthopaedist
- ☐ Radiologist
- ☐ Intensivist
- ☐ Emergency physician
- ☐ ED nurse
- ☐ Nurse from other divisions
- ☐ Radiology technician
- ☐ Other

Is there a protocol for major trauma in the hospital?

- o Yes
- o No

Is there a protocol for massive transfusion in the hospital?

- o Yes
- o No

Resources available in the ED

- ☐ Pelvic stabiliser (e.g. T-POD)
- ☐ Radiotranslucent bed
- ☐ High-flux fluid heater (e.g. Level 1)
- ☐ High-flow vascular catheter
- ☐ At least 3 concentrated blood units
- ☐ None of the above

eCREAM Use Case Study 1

Propensity to hospitalize patients from the ED in European centers

An observational retrospective quality-of-care study

ANNEX 3

Variables to collect:

All patients

Version 5.0, 15 April 2024

Ranica, Italy

clinicaltrials.gov n: NCT06354764

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VARIABLES TO COLLECT FOR EACH PATIENT:

- Date and time of arrival at the ED
- Mode of arrival
- Age
- Triage code
- Date and time of nurse's taking on of the patient
- Date and time of doctor's taking on of the patient
- Date and time of the decision to transfer to Short Stay Observation Unit (OBI)
- Date and time of the decision to admit/transfer to another hospital/discharge
- Date and time of transfer to OBI
- Date and time of exit from ED/OBI
- Mode of exit (admitted/transferred/deceased/voluntary abandonment)

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ANNEX 4

Virtual case report form:

Dyspnea and TLOC

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1. **DYSPNEA**

1.1 Demographic

- Sex [male/female]
- Age [number]

1.2 History taking

- History of allergy [yes/no]
- History of recent trauma [yes/no]
- Pregnancy [yes/no]
- Presence of chronic pulmonary disease (either obstructive or restrictive) [yes/no]
- Chronic organ failure (respiratory, cardiac, renal, metabolic) [yes/no]
- Diffuse vascular disease [yes/no]
- Chronic rheumatologic disease [yes/no]
- Active neoplasia [yes/no]
- Chronic dialysis [yes/no]
- Immunosuppression [yes/no]
- Palliative care [yes/no]
- Neuropsychiatric disorders [yes/no]
- Poly-pharmacological therapy [yes/no]
- Problematic family context [yes/no]
- Need but absence of a caregiver [yes/no]
- Homelessness [yes/no]
- Living alone [yes/no]

1.3 Clinical examination

- Dementia [yes/no]
- General condition deterioration [yes/no]
- Level of autonomy (mobility) [4 levels: walking independently, walking with auxiliary aids, walking with physical assistance, bedridden]
- Level of consciousness [4 levels: AVPU]
- Agitation [yes/no]
- Presence of respiratory distress [yes/no]
- Foreign body in the airways [yes/no]
- Respiratory rate [number]
- Body temperature [number]
- Heart rate [number]
- Blood pressure [number]
- Improvement of dyspnea [yes/no]

1.4 Lab test results

- SpO_2 [number]
- pH [number]
- PaO_2 [number]
- $PaCO_2$ [number]
- HCO_3^- [number]
- Lactates [number]
- Hemoglobin [number]
- Platelets [number]
- Leukocytes [number]
- C-Reactive Protein [number]
- Blood sodium [number]
- Blood potassium [number]
- Blood glucose [number]
- Creatinine [number]
- Transaminases [number]
- INR [number]
- Troponin [number]
- BNP / NT-pro-BNP [number]
- D-dimer [number]
- SARS-CoV-2 swab test [pos/neg]

1.5 Imaging test results

- Thoracic ultrasound, any abnormalities [yes/no]
- ECG, any abnormalities [yes/no]
- Head/neck CT, any abnormalities [yes/no]
- Chest CT, any abnormalities [yes/no]
- Chest Rx, any abnormalities [yes/no]
- Gastroscopy [yes/no]

1.6 Treatment

- Performance of thoracentesis [yes/no]
- Administration of diuretics [yes/no]
- Administration of steroids [yes/no]
- Administration of bronchodilators [yes/no]
- Administration of oxygen/ventilation [yes/no]
- Blood transfusions [yes/no]

1.7 Final diagnosis

- Situational syncope [yes/no]

- Pulmonary embolism [yes/no]
- Heart failure [yes/no]
- Pneumonia [yes/no]
- COPD exacerbation [yes/no]
- Acute pulmonary edema [yes/no]
- Asthma exacerbation [yes/no]
- Severe Anemia [yes/no]
- Arrhythmia [yes/no]
- Respiratory failure [yes/no]
- Intoxication [yes/no]
- COVID 19 [yes/no]
- Influenza and various infections [yes/no]
- Pneumothorax [yes/no]
- Acute coronary syndrome [yes/no]

1.8 Follow-up

- 30-day mortality [dead/alive] (if possible)

2. **TRANSIENT LOSS OF CONSCIOUSNESS**

2.1 Demographic

- Sex [male/female]
- Age [number]

2.2 History taking

- History of drug abuse [yes/no]
- History of alcohol abuse [yes/no]
- Presence of pacemaker [yes/no]
- Presence of defibrillator [yes/no]
- Cardio-pulmonary resuscitation [yes/no]
- Antihypertensive therapy [yes/no]
- Anticoagulants or antiplatelet drug therapy [yes/no]
- Diagnosis of cardiovascular diseases [yes/no]
- Diagnosis of neurodegenerative diseases [yes/no]
- Diagnosis of peripheral neuropathy [yes/no]
- Pregnancy [yes/no]
- Diagnosis of Chronic respiratory failure [yes/no]
- Diagnosis of Chronic cardiac failure [yes/no]
- Diagnosis of Chronic renal failure [yes/no]
- Diagnosis of Chronic metabolic failure [yes/no]

- Diagnosis of Diffuse vascular disease [yes/no]
- Diagnosis of Chronic rheumatologic disease [yes/no]
- Active neoplasia [yes/no]
- Chronic dialysis [yes/no]
- Immunosuppression [yes/no]
- Palliative care [yes/no]
- Neuropsychiatric disorders [yes/no]
- Poly-pharmacological therapy [yes/no]
- Speed with which the patient recovered consciousness [2 levels: fast (seconds)/slow (minutes-hours)]
- Presence of prodromal symptoms [yes/no]
- Compliance with antiepileptic therapy [yes/no]
- Duration of the patient's unconsciousness [2 levels: short (seconds)/long (minutes-hours)]
- TLoC during effort [yes/no]
- TLoC while supine [yes/no]
- First episode vs. known history of epilepsy [yes/no]
- Antiepileptic therapy already in place [yes/no]
- Drowsiness, confusion, disorientation as postcritical state [yes/no]
- Pale skin during the episode [yes/no]
- Eye deviation during the episode [yes/no]
- Stiffness during the episode [yes/no]
- Drooling during the episode [yes/no]
- Tonic-clonic seizures [yes/no]
- Situation description, like coughing, prolonged periods of straining, sudden abdominal pain, phlebotomy [yes/no]
- Problematic family context [yes/no]
- Need but absence of a caregiver [yes/no]
- Homelessness [yes/no]
- Living alone [yes/no]

2.3 Clinical examination

- Dementia [yes/no]
- General condition deterioration [yes/no]
- Level of autonomy (mobility) [4 levels: walking independently, walking with auxiliary aids, walking with physical assistance, bedridden]
- Level of consciousness [4 levels: AVPU]
- Agitation [yes/no]
- Presence of dyspnea [yes/no]
- Body temperature [number]
- Heart rate [number]
- Blood pressure [number]

- Chest pain [yes/no]
- Head or other districts trauma [yes/no]
- Ab ingestis pneumonia [yes/no]
- Tongue bite [yes/no]
- Further seizures in the ED [yes/no]
- Blood in the stool [pos/neg]
- Carotid sinus massage [yes/no]
- Supine-to-standing systolic blood pressure test [yes/no]
- Improvement of patient's conditions [yes/no]
- Neurologist consultation [yes/no]

2.4 Diagnostic test results

- ECG, any abnormality [yes/no]
- ECG monitoring, any abnormality [yes/no]
- EEG, any abnormality [yes/no]

2.5 Lab test results

- SpO_2 [number]
- Lactates [number]
- Hemoglobin [number]
- Platelets [number]
- Leukocytes [number]
- C-Reactive Protein [number]
- Blood glucose [number]
- Blood sodium [number]
- Blood potassium [number]
- Blood calcium [number]
- Creatinine [number]
- Transaminases [number]
- INR [number]
- Troponin [number]
- BNP / NT-pro-BNP [number]
- D-Dimer [number]
- Serum creatine kinase [number]
- Blood alcohol [number]
- Blood drug dosage [number]
- Urine drug test [number]

2.6 Imaging test results

- Brain CT scan, any abnormality [yes/no]

- Brain MRI, any abnormality [yes/no]
- Cardiac ultrasound, any abnormality [yes/no]
- Chest CT scan, any abnormality [yes/no]
- Pulmonary scintigraphy, any abnormality [yes/no]
- Gastroscopy [yes/no]
- Abdomen CT scan, any abnormality [yes/no]
- Doppler ultrasound of deep veins, any abnormality [yes/no]
- Compression ultrasound (CUS), any abnormality [yes/no]

2.7 Treatment

- Administration of fluids [yes/no]

2.8 Final diagnosis

- Situational syncope [yes/no]
- Epilepsy / epileptic seizure [yes/no]
- Pulmonary embolism [yes/no]
- Arrhythmia [yes/no]
- Cardiac tamponade [yes/no]
- Aortic dissection [yes/no]
- Acute coronary syndrome [yes/no]
- Hemorrhage [yes/no]
- Severe Anemia [yes/no]
- Concussive head trauma [yes/no]

2.9 Follow-up

- 30-day mortality [dead/alive] (if possible)

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ANNEX 5

Data processing and protection

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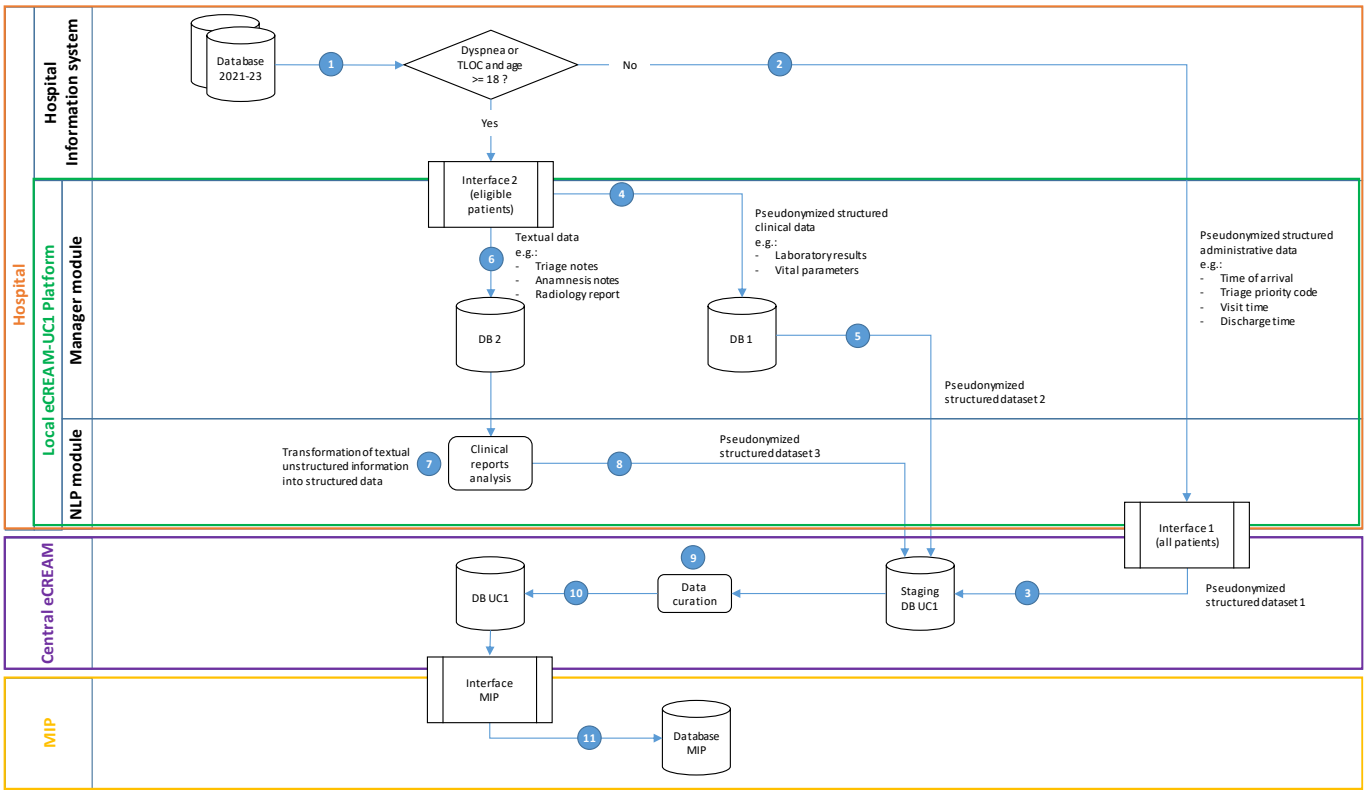
1. DATA PROCESSING

The processing of data collected in the context of Use Case Study 1 of the eCREAM project (eCREAM-UC1) has been planned with the specific aim of protecting, to the highest possible level, the privacy of the patients involved. The figure reproduced below outlines the processing of data that will be carried out.



The first data processing session will take place within the information systems of the participating hospitals (*Hospital* in the diagram above), where the eCREAM platform specially developed for the project will be installed (*Local eCREAM-UC1 Platform*).

The first step will be to identify patients eligible for extended data collection (i.e., adults who accessed the ED for dyspnea or loss of consciousness) starting from the data filled in at triage. The hospital information system managers will be in charge of this step. For non-eligible patients, pseudonymized information needed to calculate, at any given moment, the number of patients in the ED, the timing of some specific steps in the patient's clinical pathway, and other details will be transferred using secure protocols (second step) to the study's central server, through a specific interface (*Interface 1* in the diagram). The pseudonymization code (or pseudonym) will be chosen by the hospital information system administrator. These data, primarily administrative in nature, will populate a staging database (*Staging DB UC1*) within the eCREAM central server (third step). Annex 4 of the protocol provides the complete list of data to collect.

In the fourth step, for eligible patients, a specific interface (*Interface 2*) will populate the *DB 1* with the information already structured in the available sources that are required in the study's data collection form (virtual case report form, vCRF, see Annex 4). This information involves the laboratory test results provided in the vCRF and any other structured fields in the ED program in use (e.g., vital parameters). These data will then be transferred to the eCREAM's central server, where they will be merged with dataset 1 in the *Staging DB UC1* (fifth step).

In the sixth step, *Interface 2* will transfer all textual information about eligible patients to *DB 2*. By textual information,

we mean both the notes in the ED programs (e.g., those in the clinical examination section) and the documents produced by other programs (e.g., radiology reports). At this stage, the NLP algorithm, developed especially for the project and integrated into the locally installed eCREAM platform, will come into play (*Clinical reports analysis*), with the task of transforming the textual, unstructured information into the structured clinical data provided by the vCRF (step 7).

The eighth step refers to the transfer of the data thus obtained to the eCREAM project's central server, where they will become part of *Staging DB UC1* to complete the data collection and enable *Data curation* (step 9). This step consists of checking and correcting any problems with individual center data, performing additional data harmonization, and populating the final database for analysis (*DB UC1*, step 10).

Finally, an additional interface (*Interface MIP*) will transform the DB UC1 into a flat file (two-dimensional database) that will be transmitted to the MIP (Medical Informatics Platform, step 11). The MIP is the data-sharing platform used in eCREAM to enable secondary use of data (see section 2.5 for MIP details).

By adopting this data processing plan, the principle of minimization will be ensured, as only data necessary for the pursuit of the study objectives will be transmitted from the participating centers to the study coordination center.

2. TECHNICAL ASPECTS OF DATA PROCESSING AND PROTECTION

2.1. Data Transmission

2.1.1. Exposure of APIs on the local eCREAM platform

Integration APIs between hospital systems and local eCREAM components will be exposed not on the internet but on the intranet. Thus, transmission of data that has not yet been pseudonymized will occur over the hospital's internal network.

2.2. Authentication

In order to invoke one or more APIs, the ED system must be an application surveyed by eCREAM, which will receive from eCREAM the authentication credentials needed by the application in the Access Token request phase; this Token will have to be attached to each subsequent API invocation.

The application's credentials must not be disclosed or reused to build other applications. Each new application must be individually registered so that they will be issued the corresponding credentials.

It will be the user's responsibility to properly protect the credentials used by the various application instances.

eCREAM will verify that the credentials used for each integration API access with the local eCREAM system are associated with the previously surveyed hospital network.

Regarding access to the Integration API with central eCREAM, the eCREAM system will verify with each connection that the credentials are associated with a certificate issued by eCREAM and installed on the calling machines.

The Access Token will be obtained by calling a special API in the eCREAM system.

An Access Token will have a limited life of 30 minutes so, when it expires, it will have to be renewed through the appropriate API of the eCREAM system.

2.2.1. Authorization

Access to the API will be subject to an authorization system that leverages the authentication features described above.

API access will be associated with compartmentalization criteria called *scope*.

When a hospital application is censored in eCREAM, the roles required to use the corresponding scopes will be associated.

When issuing the Access Token, the Authentication API requires the caller to specify the list of scopes associated with the API/resources it will use through that Token, or else authorization in accessing the API will be denied at the point of fruition.

2.2.2. Logging and Tracking API Accesses.

All interactions between the application and external systems will generate a record in the application log.

The log will not contain sensitive data, but only data related to system operations or incidents captured by the system.

It will allow identification of the calling user or system, the operation with the metadata necessary to verify whether the operation in question affected a specific dataset of sensitive data and the timestamp of the operation.

This will make it possible to identify abusive or attempted access to data.

2.3. **Data processing in the local eCREAM system**

The components that make up the local eCREAM system are entirely installed within the server farms operated by hospital entities.

The local eCREAM components will receive sensitive data associated with subject identification data contained in free text fields and clinical documents.

The data processing procedure involves transmitting the data to the local eCREAM components, which will provide further processing and subsequent transmission, in pseudonymized form, to the central eCREAM platform.

2.3.1. Pseudonymization

Already pseudonymized data will be transferred from the hospital information system to the local eCREAM platform. The hospital information system administrator will choose the pseudonymization code (or pseudonym).

2.3.2. Storage and retention of pseudonymized data within the local eCREAM platform

Databases and file systems that store pseudonymized data within the local eCREAM platform will be encrypted. Data will be retained in such archives only as long as necessary for further processing and subsequent transmission to the central eCREAM components. At the end of the transmission process, the data will be physically deleted.

2.3.3. Physical access control

With regard to the central eCREAM components, physical access control will be the responsibility of the hospital entity, the data controller.

2.3.4. Logical access control

Data access will be allowed only to system administrators. Control will be performed by configuring the enabled connection IPs and verifying the validity of the required certification associated with the individual enabled IP.

Access will be conveyed via VPN and allowed only through personal credentials provided only to administrators appointed to process the data.

2.3.5. Logging, tracking of access and activities performed

All interactions between the application and external systems, including system administrators, will generate a record in the application log.

The log will not contain sensitive data, but only those related to operations performed through the system or incidents captured by the system.

It will allow identification of the calling user or system, the operation with metadata necessary to verify whether the operation in question affected a specific dataset of sensitive data, and the timestamp of the operation.

This will help identify any abusive access or attempts to access data.

2.3.6. Antivirus

The local eCREAM system will allow files to be transmitted to it, so a server-side antivirus will be provided to scan incoming files.

2.4. **Data processing in central eCREAM**

2.4.1. Data storage

Databases and file systems will be encrypted.

2.4.2. Data retention

The data collected in eCREAM-UC1 will be centrally stored on the central eCREAM server (and on the MIP) for 20 years from the study closure date. The eCREAM project's central server is located in Milan, Italy. At that point, all data collected for eCREAM-UC1 will be permanently deleted. Should the data be considered of particular interest for other scientific purposes, specific authorization will be requested from the competent ethical authorities to extend the duration of the storage.

2.4.3. Backup

Processed data will be backed up daily via a fully automatic process, with a 30-day data retention period.

Backup databases and file systems will be encrypted.

2.4.4. Physical access control

Data will be processed exclusively through a cloud server service. The server farm is ISO 27018 certified, a code of conduct for personal data security in the cloud and includes physical access control to eCREAM delivery machines, among other aspects.

2.4.5. Logical access control

Data access will be allowed only to system administrators. Control will be performed by configuring the enabled connection IPs and verifying the validity of the required certification associated with the individual enabled IP.

Access will be allowed on a nominal basis to system administrators, authorized only through access machines having registered certificates and authorized IP.

2.4.6. Logging, tracking of access and activities performed

All interactions between the eCREAM application and external systems, including system users, will generate a record in the application log.

The log will not contain sensitive data, but only data related to operations performed through the system or incidents captured by the system.

It will allow identification of the calling user or system, the operation with metadata necessary to verify whether the

operation in question affected a specific dataset of sensitive data, and the timestamp of the operation. This will help identify any abusive access or attempts to access data.

2.4.7. Antivirus

The system will use a server-side antivirus to keep the delivery environment scanned.

2.5. **The Medical Informatics Platform (MIP)**

The MIP is the data sharing platform used in eCREAM to fulfill the project's aims to FAIRIFY its data (i.e., make data Findable, Accessible, Interoperable, and Reusable). The MIP is an open-source, GDPR-compliant, privacy-aware platform enabling remote and federated analyses from datasets physically distributed in various hospitals, research centers, and biobanks, without moving the data outside their original site of storage to a central repository. The MIP is installed on the EBRAINS server developed in the Human Brain Project (HBP) by the Centre Hospitalier Universitaire Vaudois (CHUV), an eCREAM partner. The EBRAINS server is a cluster of physical servers located at the Centro Svizzero di Calcolo Scientifico (CSCS) in Lugano, Switzerland.

Once the data collected in eCREAM's central database are transmitted to the MIP, access to them will be controlled by the MIP's security system. Through authorization mechanisms, this system will enable the precise definition of which data will be made available to each user and with which level of access, providing full control over data access and analyses. See https://mip.ebrains.eu for more technical documentation on the MIP.

eCREAM Use Case Study 1

Propensity to hospitalize patients from the ED in European centers

An observational retrospective quality-of-care study

ANNEX 6

Study information for institutional websites

Version 5.0, 15 April 2024

Ranica, Italy

clinicaltrials.gov n: NCT06354764

eCREAM Coordinating Center
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Informativa sulla partecipazione del pronto soccorso al progetto eCREAM
(disponibile sul sito dell'azienda ospedaliera)

Cos'è il progetto eCREAM?

Il progetto eCREAM (enabling Clinical Research in Emergency and Acute care Medicine) ha l'obiettivo di sviluppare soluzioni tecnologiche innovative per facilitare la conduzione di progetti di ricerca clinica nei Pronto Soccorso italiani ed europei. La ricerca clinica serve sia a studiare l'efficacia dei trattamenti e degli esami diagnostici per curare meglio i pazienti, sia a valutare e migliorare la qualità dell'assistenza che i singoli reparti sono in grado di garantire ai propri pazienti. Il progetto eCREAM mira allo sviluppo di nuove soluzioni per ricavare informazioni cliniche accurate e affidabili da diversi tipi di fonti di dati già utilizzate durante l'attività dei Pronto Soccorso, ad esempio le cartelle cliniche, per colmare il divario fra il bisogno di ricerca e la possibilità di realizzarla.

Chi è il promotore e chi partecipa al progetto eCREAM?

Il Progetto eCREAM è coordinato dall'Istituto di Ricerche Farmacologiche Mario Negri IRCCS, ente morale senza scopo di lucro nato nel 1961, che opera nel campo della ricerca biomedica al servizio della salute pubblica attraverso la realizzazione di progetti di ricerca scientifica, la formazione di giovani e la diffusione dei risultati della ricerca. L'Istituto è indipendente rispetto a interessi commerciali, partiti politici, credo religiosi e sceglie di non brevettare le proprie scoperte per metterle a disposizione di tutti, e non ha altra finalità che quella di ricerca scientifica.

Per ulteriori informazioni: www.marionegri.it

Il consorzio del progetto eCREAM include 11 partner con competenze cliniche, tecniche e scientifiche in 8 paesi europei (Francia, Grecia, Italia, Polonia, Slovacchia, Slovenia, Svizzera e Regno Unito).

Per ulteriori informazioni: https://ecreamproject.eu/

Da chi è finanziato il progetto eCREAM?

Il progetto è supportato da fondi pubblici europei. È stato finanziato dalla Commissione Europea (nell'ambito del programma Horizon Europe, contratto n. 101057726), nonché da UKRI (United Kingdom Research and Innovation) e SERI (Swiss State Secretariat for Education, Research and Innovation) per un totale di 8,710,124 €.

Cosa significa che questo Pronto Soccorso partecipa al progetto eCREAM?

Questo Pronto Soccorso, partecipando al progetto eCREAM, contribuisce alla costruzione di un database di dati clinici e amministrativi che consentirà di studiare la propensione dei medici di Pronto Soccorso a ricoverare i pazienti. Esiste infatti una certa variabilità fra medici nella decisione di ricoverare o meno i pazienti, ed è importante studiare questa variabilità per migliorare l'intero processo di cura.

Anche se lo studio si concentra su alcune tipologie di diagnosi all'ingresso del pronto soccorso, la decisione di ricoverare o dimettere un paziente dipende da molte variabili che possono essere stimate correttamente solo avendo a disposizione alcune informazioni raccolte su tutti i pazienti giunti in Pronto Soccorso. I dati utili per lo studio verranno raccolti a partire dalle cartelle cliniche dei pazienti che si sono presentati al Pronto Soccorso **dal 1 gennaio 2021 al 31 dicembre 2023** e saranno trasferiti al centro di coordinamento dello studio in forma pseudonimizzata. Ciò significa che i dati trattati verranno privati di elementi identificativi, così che per il personale che farà le analisi non sarà possibile risalire all'identità (nome e cognome) dei pazienti cui i dati si riferiscono. Le elaborazioni statistiche prodotte dal progetto eCREAM conterranno solo dati aggregati senza alcun riferimento a specifici pazienti.

Quali autorità hanno valutato e approvato lo studio eCREAM?

Il protocollo dello studio eCREAM è stato approvato dai comitati etici di tutti i centri partecipanti, fra cui anche quello nel nostro Pronto Soccorso.

Il Garante per la Protezione dei Dati Personali ha dato parere favorevole al trattamento dei dati raccolti per il progetto eCREAM ai sensi dell'art. 9, paragrafo 2, lettera j) del Regolamento UE 2016/679 e dell'art. 2-sexies, comma 2, lett. v) del decreto legislativo n. 196/2003 per finalità di programmazione, gestione, controllo e valutazione dell'assistenza sanitaria in regime di emergenza urgenza.

Chi è il titolare del trattamento dati?

Titolare del trattamento dei dati è l'Istituto di Ricerche Farmacologiche Mario Negri IRCCS, coordinatore del progetto eCREAM. Per la realizzazione del progetto eCREAM il titolare ha designato Astir s.r.l. (https://www.astir.com/) quale responsabile del trattamento ai sensi dell'art. 28 del Regolamento (UE) 2016/679.

Il titolare ha inoltre individuato un responsabile della protezione dei dati, contattabile al seguente indirizzo: privacy@marionegri.it

Dove posso richiedere chiarimenti ed esercitare i miei diritti secondo il Regolamento Europeo per la protezione dei dati personali?

In relazione al trattamento dei dati personali, la vigente normativa riconosce all'interessato la facoltà di esercitare tutti i diritti previsti dagli artt. da 15 a 22 del Regolamento (UE) 2016/679, tra cui:

1. il diritto di ottenere: a) la conferma che sia o meno in corso un trattamento di dati personali e, in tal caso, di ottenere l'accesso ai dati personali e alle informazioni previste dalla citata normativa; b) la rettifica dei dati personali inesatti, l'integrazione di quelli incompleti; c) la cancellazione dei dati, salvo i casi previsti dalla vigente normativa; d) la limitazione del trattamento, nei casi previsti dalla legge; e) la portabilità dei dati, in caso di dati personali raccolti sulla base del consenso e trattati con mezzi automatizzati.
2. Il diritto di opporsi in qualsiasi momento, per motivi connessi alla sua situazione particolare, al trattamento dei dati personali che lo riguardano, salvo le situazioni previste dalla normativa.
3. Il diritto di proporre reclamo all'Autorità Garante per la Protezione dei dati personali.

I diritti di cui sopra potranno essere esercitati scrivendo al titolare del trattamento: Istituto di Ricerche Farmacologiche Mario Negri, Ranica BG 24020, Italia, e-mail: fenice@marionegri.it oppure contattando il responsabile della protezione dei dati al seguente indirizzo mail: privacy@marionegri.it