Adverse event prediction in Geriatric patients in the ED with Ultrasound

AGEDU

Research register number: 202100945

(non-WMO study protocol to obtain data/biomaterials from the Acutelines biobank)

Date of protocol: **24-11-2021**
Version number: **1.3**

List of abbreviations and relevant definitions

ED	Emergency Department
UMCG	University Medical Centre of Groningen
APOP	Acutely Presenting Older Patient
MRI	Magnetic resonance imaging
CT	Computed Tomography
Qcsa	Cross-sectional area
CFS9	Clinical Frailty Scale
METC	Medical research ethics committee (MREC); in Dutch: medisch ethische toetsing commissie (METC)
Sponsor	The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.
WMO	Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen)
LOS	Length of stay
ITU	Intensive therapy unit
eCRF	Electronic consent form
REDCap	Research electronic Data Capture

CONTENT

1. STUDY ORGANIZATION

Study title	Acutelines: Adverse event prediction in Geriatric patients in the ED with Ultrasound (research register number 202100945)
Planned start date	01-01-2022
Estimated completion date	01-10-2022
Project leader (UMCG)	Dr. E. ter Avest, Emergency physician University Hospital Groningen, University of Groningen Department of Emergency Medicine Email: e.ter.avest@umcg.nl
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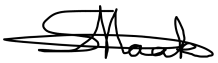
Corresponding researcher UMCG	S.L. Haak, AIOS Emergency Medicine Emergency Medicine Department Email: s.l.haak@umcg.nl Phone: 06-46771836
Sponsor (in Dutch: verrichter/opdrachtgever)	UMCG (Acutelines)
Financial support/subsidising party	**Geldstroom**: • NA
Collaboration with non-profit Laboratory / research sites (in- and outside UMCG)	NA
Collaboration with commercial parties / companies (in- and outside UMCG)	NA
Name bio- or databank and bankmanager	**Acutelines** (research register number 201900635) Center for Acute Care UMCG Email: acutelines@umcg.nl Phone: 68943 Manager: prof.dr. B.C. van Munster, internal medicine Project leader: dr. H.R. Bouma, internal medicine ☒ approved by the Board of Directors UMCG ☐ not approved by the Board of Directors UMCG
Name previous study ('FAIR data')	Acutelines

2. PROTOCOL SIGNATURE SHEET

The undersigned (Principal) investigator and head of department UMCG confirm that the study and its procedures will comply with the present study protocol and the nWMO Kaderreglement UMCG, and in addition agree with the Acutelines regulations for further use of data and biomaterials as stated in the current document. Without ethical approval the data/biomaterials will not be used for other (research) purposes (e.g. 'FAIR data').

Name	Signature	Date
(Principal) investigator UMCG:	 S.L. Haak, AIOS Emergency Medicine	21-01-2022
Head of the department UMCG:	 Prof. Dr. JC ter Maaten, acute internal medicine physician	21-01-2022
Bank manager Acutelines	 Prof.dr. B.C. van Munster	21-01-2022
Steering group Acutelines	 Dr. H.R. Bouma	21-01-2022

3. ABSTRACT (max. 250 words)

- **Background**

Older people visit the ED more frequently then younger people and have a higher risk of functional decline, ED revisit or death. Several screening tools (such as VMS and APOP) have been developed to identify patients at the highest risk of adverse outcomes. Almost all require adequate communication with the patient, which is not always possible, for example when elderly patients present with a delirium. Point of Care Ultrasonography (POCUS) may be a valuable alternative screening tool in these instances.

- **Main research question**

To identify whether POCUS measurement of the rectus femoris muscle cross-sectional area (Qcsa) can be used as an alternative screening tool to predict functional decline, ED revisit or death in elderly patients in the ED.

- **Design (including population, confounders/outcomes)**

This is a single centre prospective trial. Patients >70 years and older presenting in the ED of the UMCG hospital who are participating in the Acutelines bio-databank are eligible for inclusion. 68 patients will be included. Data will be extracted from the Acutelines bio-databank. A trained physician will perform ultrasound measurements in a standardized way.

- **Expected results**

The aim of this study is to evaluate whether ultrasound measurements of the Qcsa can be utilized to identify older patients who are at risk for functional decline, ED revisit or death.

4. BACKGROUND

- **Introduction and rationale**

Older patients visit the emergency department (ED) more frequently in comparison to younger adults [1,2]. Admittance to the ED is associated with risk of negative health outcomes such as functional decline and mortality (the ultimate form of functional decline) [2,3]. This is partly explained by non-specific disease presentation or the presence of frailty, comorbidities or cognitive disorders, which complicates their ED presentation, diagnosis and management [4-6]. It is important to identify older patients with frailty, who are at the highest risk for negative outcomes, in order to be able to take appropriate measures during hospitalization (e.g. fall prevention, physiotherapy, geriatric consultation). Recently it became mandatory to screen all elderly ED patients for frailty as stated by the Health and Youth Care Inspectorate in the Netherlands.

Several geriatric screening tools have been developed to identify frail geriatric patients in the ED [7]. The Acutely Presenting Older Patient (APOP) tool has already been implemented in several Dutch hospitals [8]. This is a validated instrument to predict risk for functional decline and mortality in older patients within three months of presentation in the ED [8, 9]. Like most of the existing screening tools the APOP relies on adequate communication with the patient (or the patients' caregiver). Unfortunately, not infrequently communication with the patient is impaired in the ED due to trauma, confusion, sickness or pre-existent dementia.

An alternative screening tool, based on measurement of sarcopenia with POCUS may provide valuable information in these instances. Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death [10]. Sarcopenia and frailty are two separate conditions, but they overlap especially in the physical aspects of frailty [11]. Therefore, measuring sarcopenia might help in predicting frailty. MRI and CT are regarded as the gold standard to measure muscle mass but they are inconvenient and impossible to perform in everyday clinical practice, especially in the ED [10].

POCUS has been shown to be a promising technique to measure skeletal muscle mass [12]. It is non-invasive, can be performed at the bedside and has an excellent intra-class correlation coefficient for intra- and inter-observer agreement. [13, 14] Recent studies in a subgroup of hospitalized patients have shown that Qcsa measurements can predict readmission and mortality [15, 16]. ED data however are scarce: Shah et al found in a subset of elderly trauma patients that ultrasound measurements of biceps and quadriceps had modest concordance with the Clinical Frailty Scale (CFS9) [17], whereas Benton et al demonstrated that ultrasound measurements of sarcopenia in older non-trauma patients were (to a variable extend) associated with frailty, falls and subsequent hospitalizations [18].

As POCUS measurement of Qcsa is independent of patient effort and functional or cognitive impairment, it has the potential to be a valuable (alternative) screening tool for functional decline

and mortality in older patients in the ED. However, until now, no data have been published about the relation between Qcsa and functional outcome for patients presenting in the ED.

The aim of this study is to evaluate whether ultrasound measurements of the Qcsa in the ED may be utilized to identify older patients who are at risk for functional decline, ED revisit or death. Our study hypothesis is that Qcsa measurements can predict functional decline, ED revisit or death of older ED patients.

- **Research question**

Primary objective
To evaluate:

- The relation between POCUS measurements of the Qcsa in patients >70 presenting in the ED and ED revisit or death within three months and functional decline within twelve months of their ED visit. Functional decline in this respect is defined as at least one point increase in the Katz ADL-6 survey score or new institutionalization (higher level of assisted living) within twelve months after ED visit.

Secondary objectives
To evaluate:

- To compare the ability of the Qcsa ultrasound to predict functional decline, ED revisit or death in older patients in the ED to the APOP questionnaire (gold standard).
- To compare the added value of Qcsa ultrasound to the APOP questionnaire in the prediction of functional decline, ED revisit or death in older patients in the ED.
- To evaluate the relation between Qcsa ultrasound and physical activity (as scored by KATZ ADL-6 questionnaire).

5. METHOD

5.1 Description study design

This is a single centre prospective trial conducted in the ED of the UMCG. Data (including APOP, KATZ-ADL) will be collected from elderly patients presenting in the ED, and ultrasound measurements of the Qcsa will be obtained at the same time after consent is obtained for participation in the Acutelines bio-databank. Functional decline, ED revisit and mortality will be evaluated after three and twelve months as per Acutelines protocol.

5.2 Design

5.2.1 Mono- or multicenter study	Mono-center study, use of data/biomaterials from Acutelines (de novo biobank)	
5.2.2 Retrospective study (available data/ biomaterials only) or prospective study (data/ biomaterials from [some] participants will be collected in the future).	Retrospective study: ~~yes~~/no	Prospective study: YES (Acutelines)
Note: while Acutelines is a prospective data/biomaterial collection, additional data may be collected retrospectively.		
5.2.3 Cross-sectional or follow-up study	Cross-sectional study: yes~~/no~~	Follow-up study yes~~/no~~
All patients are screened in the ED. ED revisit and mortality will be evaluated after three months and functional decline after twelve months.		
5.2.4 Quantitative or qualitative study (click both if mixed-method)	Quantitative study yes~~/no~~	Qualitative study ~~yes~~/no
This is a quantitative study based on Qcsa measurement and screening tool data.		
5.2.4 Pilot study	~~yes~~/no	

5.3 Population

5.3.1 Inclusion and exclusion criteria	
Inclusion criteria: In order to be eligible to participate in this study, a subject must meet all of the following criteria: • Age (>70 years) • Presenting to the ED of the UMCG for one of the following specialties: internal medicine, nephrology, geriatric medicine, oncology, hematology, lung medicine, gastrointestinal/liver medicine, or emergency medicine (non-trauma). • Consent obtained for participation in the Acutelines bio-databank Exclusion criteria: • Unable to obtain ultrasound image of rectus femoris (e.g. amputation, edema) • Paresis or paralysis of one or both legs	
5.3.2 Number of participants	
• Target total number of participants: 68 • Target number of UMCG participants: 68	
5.3.3 Study subjects (tick all that apply)	
• Healthy volunteers • Patients	**~~NO~~** **YES**
5.3.4 Subject classification (tick all that apply)	
• Participants ≥ 16 years • Children between 12 and 16 years *(if applicable, written informed consent will be obtained*	**YES** **~~NO~~**

from child and both parents - if both have authority, or guardian [or parents/guardian only if incapacitated child]) • Children < 12 years *(if applicable, written informed consent will be obtained from both parents - if both have authority, or guardian)*	**NO** **NO**
5.3.5 Incapacitated adults	
Participants are incapacitated/ decisionally incompetent adults *(if applicable, written informed consent will be obtained from legal representative)*	**YES**

5.4 Recruitment and informed consent/objection

5.4.1	Retrospective study (tick all that apply) ☒ Not applicable (see section 5.2.2) ☐ Data will be copied from (electronic) patient records (e.g. 'EPD UMCG') ☒ Data/biomaterials will be obtained from an already existing internal or external (UMCG/non-UMCG) bio- or databank (see Section 1. Study organization). **Data/biomaterials will be obtained from the 'de novo' biobank Acutelines.** ☐ Data/biomaterials will be obtained from a previous study ('FAIR data' - internal/external; see Section 1. Study organization).
5.4.3 Objection (Registry)	
in case one or more participants will not be asked informed consent, the objection registry will be checked for these participants and the data from those who objected will be excluded from the analyses.	**NA**
All participants will be asked informed consent (Acutelines). The objection registry will be checked prior to the study to see if patients have withdrawn consent between enrollment and start of the study.	
5.4.4 Informed consent (IC): access to identifiable participant data	
in case one or more study team members will have access to direct/indirect identifiable participant data, informed consent will be/has been obtained for this access.	**YES**
5.4.5 IC: Collaboration with commercial parties	
In case of collaboration with commercial/profit organizations, informed consent will be/has been obtained for this type of collaboration	**YES**
5.4.6 IC: Linking with other registries	
In case the data will be linked with other registries, informed consent will be/has been obtained for this linkage(s)	**YES**
5.4.7 IC: Incidental findings	
In case there is a risk of incidental findings, informed consent will be/has been obtained to return findings to the participant	**YES**
Participants are asked (written, consent form) whether they would like to be informed about incidental findings.	
5.4.8 IC: FAIR Data	
In case data collected for the present study will be shared for future studies, informed consent will be obtained for this	**YES**
5.4.9 IC: other aspects	
NA	
5.4.10 Withdrawal	
• Can participants withdraw informed consent before publication and will all data/ biomaterials of that participant be destroyed • Does the participant information letter contain information on how to withdraw	**NO** **YES**
If data or biomaterials have already been used, it cannot be destroyed anymore as stated in the consent form.	

5.5 Research Data Management Plan (RDMP)

In this study the data will be collected, processed, and archived in accordance with the General Data Protection Regulation (GDPR) and the FAIR (Findable, Accessible, Interoperable, Reusable) principles under the responsibility of the Principal Investigator. A research data management plan (RDMP) has been drawn up to describe the further operational details and procedures.	
☒ the RDMP section below is completed ☐ a separate RDMP document will be attached to this protocol (appendix)	
5.5.1 Data collection	
• Only essential baseline characteristics and data required to answer the research question(s) will be collected (retrieved from Acutelines)	**YES/~~NO~~**
Primary outcome: Ultrasound measurement images of the rectus femoris muscle cross-sectional area and data about ED revisit or death within three months and functional decline (Katz ADL-6 survey score or new institutionalization) within twelve months of their ED visit. Secondary and other outcomes: Data from the APOP questionnaire.	
• Tooling (eg. software and procedures) used for collecting, processing, analysing, and storing data will be compliant with the UMCG policy and Standard Operating Procedures in the UMCG Research Toolbox.	**YES/~~NO~~**
5.5.2 Anonymization and pseudonymization	
• Data will be anonymised during data collection (i.e. data cannot be linked back to the participant)	**NO** (only partially)
To allow follow-up of participants through surveys and importing data from the electronic health records or external sources, data cannot be anonymised upon collection in Acutelines, but have to be stored pseudonymized.	
• Data will be pseudonymized by use of a code list stored in the electronic patient file (EPD) during data collection.	**YES**
• Indirect and direct identifiable information collected will be minimized and only collected for the purpose of this study	**YES**
• Direct identifiable information (e.g. contact details, code list/encryption key/subject identification log) will be stored separately from pseudonymized data in the electronic patient files (EPD), while the email address is stored in RedCap (field marked and protected as "identifier").	**YES**
5.5.3 Data access (during the study)	
• Direct identifiable information can only be accessed by the Principal Investigator and study delegates after authorization by the Principal Investigator.	**YES**
• Pseudonymized/anonymized data can only be accessed by the Principal Investigator and study delegates after authorization by the Principal Investigator.	**YES**
• Data roles, responsibilities, access and authorization - during the study and after study completion - will be managed and documented (e.g. in the RDMP, on study delegation log).	**YES**
5.5.4 Data sharing (during and after study completion)	
In case data (and biomaterials) will leave the UMCG, will you contact the loket Contract Research to arrange the proper contracts? (Loket_Contract_Research@umcg.nl)	**~~NA~~/YES/~~NO~~**
In case data (and biomaterials) will leave the UMCG, will you contact the Acutelines steering group and manager to arrange the proper contracts? (acutelines@umcg.nl)	**~~NA~~/YES/~~NO~~**
5.5.5 Data storage (during and after study completion)	
• Digital data will be archived on the UMCG network complying with strict UMCG security	**YES**

and back-up policy.	
• Paper source data and study files will be archived within the UMCG facilities.	**YES**
• Source data, study files and digital data will be stored 15 years after the study is completed.	**YES**
5.5.6 Data re-use and access after completion of the present study ('FAIR data')	
• Data will become available and shared for re-use and participants will be asked informed consent for this ('FAIR data')	**YES**
Acutelines stimulates re-use and access of data ("FAIR data"), which is the primary aim of Acutelines and for which participants are asked informed consent.	
• Data will be made findable by including the description of the study (and type of data (i.e. metadata) in the UMCG FAIR data catalogue and other discipline specific catalogue(s).	**YES**
Data and biomaterials are findable through the website (acutelines.umcg.nl), where a data dictionary can be found and a link to the Groningen data catalogue.	
• Review procedure, conditions and agreements for re-use of data and access to data by other researchers will be drawn up.	**YES**
These are described in the Acutelines Biobank reglement	
• For this study a discipline specific metadata standard will be chosen (i.e. to increase interoperability and re-use).	**YES**
<if no, explain>	
• All new data derived in this study will be returned to Acutelines to enrich the dataset (i.e. to increase interoperability and re-use).	**YES/~~NO~~**

5.6 Management of biomaterials

Will biomaterials be collected, processed, analyzed and/or stored for the purpose of this study	**YES**
Data and biomaterials are collected as part of Acutelines (de novo biobank)	
5.6.1 Retrospective study (see sections 1, 5.2.2, and 5.4.1) If biomaterials will be used from a secondary/further use biobank that has not been approved by the Board of Directors of the UMCG, how will be prohibited that biomaterials necessary for future diagnostic/treatment purposes will be used in the present study.	**NA**
5.6.2 Biomaterials collection	
• Only biomaterials required to answer the research question(s) will be collected	**NO**
• What biomaterials will be collected Plasma (EDTA, Li-Heparin, citrate), buffy coat (EDTA), wholeblood RNA (PAXGene), serum, urine, feces	
• How will the biomaterials be collected and processed Biomaterials are collected and processed according to the procedures as described by Acutelines.	
5.6.3 Pseudonymization and access to biomaterials	
• Does the storage unit of the biomaterials comprise information that the participant (in)directly identifies, other than the participant's number and / or the sample number.	**NO**
• Biomaterials can only be accessed by the Principal Investigator and study delegates after authorization by the Principal Investigator	**YES**
5.6.4 Sharing of biomaterials (during and after study completion)	
In case biomaterials (and data) will leave the UMCG, will you contact the loket Contract Research to arrange the proper contracts? (Loket_Contract_Research@umcg.nl)	**NA/~~yes/no~~**
5.6.5 Biomaterials storage (during and after study completion)	
• Where and how will the biomaterials be stored Biomaterials are collected and stored by Acutelines in the Central Freezer facility UMCG.	
• Biomaterials will be stored 15 years after the study is completed	**NA**
Biomaterials are collected and stored by Acutelines, for at least 15 years.	

• What will be done with the remaining biomaterials after study completion (eg. destroyed, returned to biobank/previous study, stored) Biomaterials are only collected as part of Acutelines, no extra biomaterials will be collected.	
5.6.6 Biomaterials re-use and access after completion of the present study **Note**: Acutelines stimulates re-use and access of data ("FAIR data"), which is the primary aim of Acutelines and for which participants are asked informed consent. Data and biomaterials are findable through the website (acutelines.umcg.nl), where a data dictionary can be found and a link to the Groningen data catalogue.	**NA** ☒

5.7 Burden, Risks & Benefits

• If participants are patients: Can be deviated from the standard care / diagnostic procedures (e.g. can medical treatment be postponed or limited)			**NA/~~yes/no~~**
Note: burden is minor, data and biomaterials are collected as part of Acutelines.			
• Will the participants risk any injuries and/or other discomfort when they participate in the proposed study	**Yes, minimal risk/burden** ☐	**Yes, more than minimal risk/burden** ☐	**No** ☒
Note: data and biomaterials are collected as part of Acutelines			
• Participant benefits/reward/incentives: **not applicable.**			

5.8 Incidental findings

• Is there a risk of incidental findings?	**Yes, minimal risk** ☒	**Yes, ≥ substantial risk** ☐	**No** ☐
If yes, ○ In case of incidental findings resulting from the POCUS ultrasound, patients will be referred to radiology at the time of the procedure for formal ultrasonography of their leg, and findings will be fed back to the treating physician ○ The patient will be informed of the need of a formal ultrasonography in case of incidental findings			

5.9 Data analysis

- Justification of sample size (e.g. power analysis)

The sample size is calculated based on functional decline and mortality in elderly visiting the ED. We defined functional decline as at least one point increase in the Katz ADL-6 survey score or new institutionalization (higher level of assisted living) within twelve months after ED visit. Prior research in the Netherlands found 9,5% of patients aged ≥70 year died within three months after ED visit and 30,6% experienced functional decline or mortality at 90-day follow-up [8]. With an assumed prevalence of the composed endpoint of 30%, 54 patients are needed to be able to confirm a diagnostic test accuracy with a sensitivity and specificity of >0.8 each for a predefined Qcsa cut-off value with a power of 90% and an alfa error of 0.05. To allow for loss of follow-up, 25% more patients will be recruited, resulting in a sample size of 68 patients.

- Statistical analysis

Continuous variables are expressed as mean (95% CI) when normally distributed and median with interquartile range when not normally distributed. Categorical data are presented as absolute

numbers and percentages.

There is a difference in muscle mass between man and woman. The ultrasound measured Qcsa will therefore be adjusted for sex by multiplying female Qcsa with the coefficient 1.484 (male=1) prior to analysis [15]. Diagnostic accuracy of QCSA will be presented as sensitivity and specificity of the optimum Qcsa cut-off point to separate cases (primary endpoint reached after three or twelve months) from non-cases. This optimum cut-off point is calculated as the maximum sum of sensitivity + (1-specificity) using ROC statistics (under the condition of equal costs of misqualification).

A logistic regression model will be used to evaluate whether individual Qcsa predicts functional decline, ED revisit or death. Age, comorbidity, Katz ADL-6, known dementia are defined as clinically relevant covariates and will be included in the regression model.. The predictive ability of the multivariable risk prediction models (e.g. Qcsa prediction model vs APOP prediction model) will be compared. $\chi 2$ values will be calculated for each prediction model.

A 2-sided P-value <0.05 will be considered statistically significant. Missing data are reported in the results section according to the STROBE 2015 guideline. All statistical analyses will be performed using R or SPSS 26.0 software.

5.10 Participant information after the study

Will participants be informed about the study results	**YES**
Acutelines aims to inform (former) participants, general public and health care professionals through their media channels (i.e. website, social media; LinkedIn and Twitter). Participants are informed about these media channels in the patient information brochure and via a "thank-you-for-participating-email".	

5.11 Research revenue

In case the study will result in revenues (e.g. as a result of the use of data/biomaterials or successful licensing of intellectual property or manufactured products), will you contact the loket Contract Research to arrange the proper contracts?	**YES**
Reveneus resulting from use of data/biomaterials or successful licensing of IP or manufactured products will be re-invested in the Acutelines biobank, in case no other agreements are made.	

6. Acutelines agreements

Return of investments	
• Return of investment in kind, as follows: Acutelines will be mentioned in all published work compromising this trial.	**YES/~~NO~~**
• Return of investment in cash according to the specified budget (6.1)	**NO**
<if both of the above are no, explain>	
Output	
• Sharing scientific output in the form of (a) co-authorship(s) for Dr. H.R. Bouma, Dr. E. ter Avest, Prof Dr J.C. ter Maaten and Prof Dr B van Munster	**YES~~/NO~~**
• Sharing intellectual property with Dr. H.R. Bouma for which further contracts will be signed prior to the initiation of the project	**NO**
• The required text for manuscripts (8.1) will be included in all publications arising from data or biomaterials derived from Acutelines	**YES**
• Any publication (a.o. [non]scientific manuscript, conference proceeding, presentation at conference, laid press, social media) arising from data or biomaterials derived from Acutelines will be send to acutelines@umcg.nl to obtain permission prior to publication	**YES**
Promoting outreach of results	
• Lay-person summary for website (text [100-150 words], infographic [A5, color] or animation [< 2 min.] in Dutch and English	**YES**
• Lay-person summary for Twitter in Dutch and English	**YES**

6.1 Acutelines budget for acquisition, storage and transfer

Note: this is a required section prior to submitting the protocol. Obtain this information by sending the protocol to acutelines@umcg.nl to ask the steering committee to complete the budget below.

Description	Number	Cost	Total
Data acquisition/storage	68	€ 0	€ 0
Biomaterial acquisition/storage	68	€ 0	€ 0
Preparation and transfer of data	68	€ 0	€ 0
Preparation and transfer of biomaterials	68	€ 0	€ 0
Total			**€ 0**

Costs are covered by participation costs of participating departments in the acutelines biobank

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8. APPENDICES

8.1 Required text for manuscript

“Data/ samples were obtained from the Acutelines data-, image and biobank [reference 3]. Acutelines is a prospective biobank including patients with a broad spectrum of acute conditions, aiming to facilitate interdisciplinary research on etiology and development of acute diseases with the aid of systematically collected biomaterials and medical data over various timepoints, both during the course of the patient’s disease and after recovery. A deferred consent procedure (by proxy) is in place to allow the collection of data and biomaterials prior to obtaining written consent. Clinical data, imaging data and biomaterials (i.e. blood, urine, feces, hair) are collected for patients presenting to the Emergency Department (ED) with a broad range of acute disease presentations. Bedside monitoring data (i.e. electrophysiological waveforms, vital parameters) are automatically captured and stored, and information from other data sources (such as the electronic health records of the hospital-, emergency medical services- and the general practitioner, the municipal registration, health insurance companies and the pharmacy) is securely imported. Follow up data are collected for all included patients during the first 72-hours of their hospitalization and 3-months, 1-year, 2-years and 5 years after their ED visit.”

"Biomaterials were collected if the participant had an orange or red triage-color, or was admitted because of sepsis, pneumonia or shock. Sepsis was defined based on the physician's suspicion, sepsis-2 or sepsis-3 criteria. Pneumonia was defined based on radiological evidence of pneumonia combined with the physician's suspicion of a pneumonia. Shock was defined as hypotension (systolic blood prsure < 90 mmHg or a decrease of > 40 mmHg compared to pre-existent) in combination with tachycardia (heart rate > 100 beats/minute).

Study data were collected and managed using REDCap electronic data capture tools hosted at [YOUR INSTITUTION].1,2 REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources."

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