ISRCTN52769435 https://doi.org/10.1186/ISRCTN52769435

A multidisciplinary approach to identify and analyse not only the causes but also the risk factors for increased mortality in invasive infections caused by Streptococcus pyogenes

Submission date
23/04/2026

Recruitment status
Recruiting

Registration date
24/04/2026

Overall study status
Ongoing

Last Edited
24/04/2026

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Principal investigator

Contact name
Dr Vaclava Adamkova

ORCID ID
https://orcid.org/0000-0002-7629-5365

Contact details
Ke Karlovu 2
Prague
Czech Republic
12000
+420 (0)725344741
vaclava.adamkova@vfn.cz

Type(s)
Scientific

Contact name
Dr Jan Zavora

Contact details
Ke Karlovu 2
Prague 2
Czech Republic
12000
+420 (0)224967264
jan.zavora@vfn.cz

Type(s)
Public

Contact name
Dr Gabriela Kronieslová

Contact details
Ke Karlovu 2, Praha 2
Prague 2
Czech Republic
12000
+420 (0)224967265
gabriela.kroneislova@vfn.cz

Additional identifiers

Study information

Scientific Title
A multidisciplinary investigation of molecular mechanisms and clinical risk factors predicting increased mortality in invasive Streptococcus pyogenes infections

Study objectives
1. To investigate the minimum inhibitory concentrations (MIC) of all S. pyogenes isolates for relevant antibiotics and determine whether the MIC values are higher in invasive isolates than in non-invasive ones
2. To find the virulence factor(s) of S. pyogenes responsible for the higher invasiveness into the bloodstream
3. Determine biomarkers, routinely diagnosable and available in urgent mode, that will function as prognostic
4. To evaluate disproportionate or inadequate answer of the immune system to S. pyogenes infection

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 20/06/2024, Ethics Committee of the General University Hospital in Prague (U Nemocnice 2, Prague, 12800, Czech Republic; +420 (0)224 961 111; eticka.komise@vfn.cz), ref: 47 /24 Grant AZV VES 2025

Primary study design

Observational

Secondary study design
Cohort study

Study type(s)

Health condition(s) or problem(s) studied
Streptococcus pyogenes infection

Interventions
This is a multicentre, prospective, non-interventional cohort study. The enrolment will take place in three centres in the Czech Republic. We plan to enrol 300 adult patients in total. Patients over 18 years of age with evidence of skin and soft tissue infection or unclear origin caused by S. pyogenes are enrolled in the study. In patients admitted with signs of infection and possible streptococcal aetiology, blood cultures are taken, standard biomarkers are collected. Patients are assigned a protocol number so that blood samples can be preserved for possible further analysis if the aetiology of S. pyogenes is confirmed.

S. pyogenes is identified by latex agglutination and matrix-assisted laser desorption and ionization time-of-flight mass spectrometry. For all strains of S. pyogenes isolated from patients with invasive infection, minimum inhibitory concentration of selected antibiotics will be determined by gradient strip method. To identify virulence factor(s), molecular genetic approaches including whole genome sequencing, transcriptomics and comparative proteomics will be used.
Biomarkers and immunological markers levels are measured in a hospital laboratory using commercially available assays as part of routine care. In the case of a confirmed S. pyogenes aetiology, biomarkers and special immunological markers will be tested from stored samples.

Intervention Type
Other

Primary outcome(s)
1. S. pyogenes identification measured using latex agglutination and matrix-assisted laser desorption ionisation at a single timepoint

2. The minimum inhibitory concentrations (MIC) of all S. pyogenes isolates for relevant antibiotics (penicillin, erythromycin, clindamycin, tetracycline, rifampicin, linezolid, co-trimoxazole, vancomycin and daptomycin) measured using gradient strip at a single timepoint

3. The virulence factor(s) of S. pyogenes responsible for the higher invasiveness into the bloodstream, measured using molecular genetic approaches including whole genome sequencing (WGS) using next-generation sequencing (NGS) technologies, transcriptomics and comparative proteomics, at a single timepoint

4. Procalcitonin (PCT), C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), white blood cell (WBC) count, Intensive Care Infection Score (ICIS), albumin, lactate, creatinine, myoglobin measured using commercially available assays as part of routine care in hospital laboratory at a single timepoint

5. Mid-regional pro-adrenomedullin (MR-proADM) and vitamin D measured using chemiluminescence immunoassay (CLIA) by Liaison XL at a single timepoint

6. Heparin-binding protein measured using enzyme-linked immunosorbent assay kit at a single timepoint

7. Pancreatic stone protein measured using point-of-care testing (POCT) at a single timepoint

8. Vascular endothelial growth factor (VEGF) measured using enzyme-linked immunosorbent assay kit at a single timepoint

9. Presence of activating molecules on selected immune cells of naïve immunity in whole blood (CD64 on neutrophils, CD169 on monocytes) measured using flow cytometry at a single timepoint

10. Activation of cell-specific immunity in human whole blood samples measured using flow cytometry at a single timepoint

Key secondary outcome(s))

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Aged >18 years
2. Invasive S. pyogenes infections
3. Skin and soft tissue infections caused by S. pyogenes

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Aged <18 years
2. Other bacterial finding in blood cultures and clinically valid samples than S. pyogenes

Date of first enrolment
23/05/2025

Date of final enrolment
30/06/2028

Locations

Countries of recruitment
Czech Republic

Sponsor information

Organisation
General University Hospital in Prague

ROR
https://ror.org/04yg23125

Funder(s)

Funder type

Funder Name
Ministerstvo Zdravotnictví Ceské Republiky

Alternative Name(s)
Ministry of Health of the Czech Republic, MZCR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Czech Republic

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available