ISRCTN68194223 https://doi.org/10.1186/ISRCTN68194223

Measuring quality of life in patients with resistant bacterial infections (part of developing the tools to fight drug-resistant bacteria)

Submission date
16/03/2022

Recruitment status
Recruiting

Registration date
21/03/2022

Overall study status
Ongoing

Last Edited
09/04/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Antibiotic resistance is one of the foremost concerns of modern medicine. While antibiotics have saved countless lives, emerging resistant bacteria (for which many antibiotics do not work) are endangering the well-being of future generations. We need to take action to reduce the effects of these infections. However, healthcare budgets are limited and we need to ensure the programmes in hospitals are providing value, especially in publically funded healthcare. To be able to justify potentially expensive measures that prevent infections with these bacteria, we need to better understand the (long-term) impact of these infections on the quality of life of patients. The REVERSE-QoL study is contained within the larger REVERSE study (ISRCTN12956554) which aims to accurately measure the quality of life in patients with and without infections with resistant bacteria.

Who can participate?
Adult inpatients aged 18 years and over admitted to participating wards in the 24 hospitals

What does the study involve?
Short questionnaires will be filled out by the participant or their representative. These questionnaries will be repeated at 1, 3, 6, and 12 months to see if the participants' quality of life changes.

What are the possible benefits and risks of participating?
The risks are small as this is an observational study. The participant or representative may experience some anxiety recalling the hospital stay or how it impacted their lives. There are no direct benefits to the participants or their representatives, but this information can be used to help patients in the future.

Where is the study run from?
University of Zurich (Switzerland)

When is the study starting and how long is it expected to run for?
July 2021 to June 2026

Who is funding the study?
European Union Horizon 2020 research and innovation programme

Who is the main contact?
Ashlesha Sonpar
reverse@usz.ch

Contact information

Type(s)
Scientific

Contact name
Dr Ashlesha Sonpar

ORCID ID
https://orcid.org/0000-0003-1676-1384

Contact details
University Hospital Zurich
Clinic for Infectious Diseases and Hospital Hygiene
Rämistrasse 100
Zurich
Switzerland
8091
+41 (0)44 255 4310
ashlesha.sonpar@usz.ch

Type(s)
Scientific

Contact name
Dr Koen Pouwels

ORCID ID
https://orcid.org/0000-0001-7097-8950

Contact details
Nuffield Department of Population Health
Richard Doll Building
Old Road Campus
Oxford
United Kingdom
OX3 7LF
+44 (0)749 046 3358
koen.pouwels@ndph.ox.ac.uk

Type(s)
Principal investigator

Contact name
Dr Walter Zingg

Contact details
University Hospital Zurich
Clinic for Infectious Diseases and Hospital Hygiene
Rämistrasse 100
Zurich
Switzerland
8091
+41 (0)43 253 03 52
walter.zingg@usz.ch

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
965265

Study information

Scientific Title
pREVention and management tools for rEducing antibiotic Resistance in high prevalence SEttings: Quality of Life study (REVERSE QoL)

Acronym
REVERSE QoL

Study objectives
To enable comparisons between different, potentially unrelated, interventions competing for the same budget ideally health-economic analyses would be expressed in terms of cost per quality-adjusted life year(QALY). This allows for maximising the quality of life of the population given a fixed budget by prioritising interventions that cost less per QALY and are affordable given the budget. QALYs represent a measure of both morbidity and mortality. However, there is a severe lack of data on the impact of different infections of interest on morbidity, as measured by health-related quality of life.

To address this knowledge gap, a matched cohort study (REVERSE-QoL) will be nested in the randomised trial with the primary objective of estimating the impact of hospital-acquired infections caused by carbapenem-resistant enterobacteriales (CRE), carbapenem-resistant

Pseudomonas aeruginosa (CRPA), or carbapenem-resistant Acinetobacter baumannii (CRAB) on patients' health-related quality of life (HRQoL) during their hospitalisations and 1-, 3-, 6-, and 12-months after their infection.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/01/2022, Kantonale Ethikkommission (Stampfenbachstrasse 121, 8090 Zürich, Switzerland; +41 (0)43 259 79 70; info.kek@kek.zh.ch), ref: AO-2021-00078

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Antimicrobial resistance and health-related quality of life

Interventions
Using a matched cohort study nested in the RCT (REVERSE - ISRCTN12956554) the researchers will compare quality of life among patients acquiring key pathogens of interest versus patients with a similar reason for admission (randomly sampled from the same ward) to estimate the impact of acquiring these infections on quality of life during the hospitalisation and 1, 3, 6, and 12 months post-discharge using EuroQol-5D (EQ-5D) and 36-Item Short-Form Health Survey (SF-36) health-related quality of life questionnaires. These validated questionnaires are available in local languages (Italian, Romanian, Greek and Spanish) and English for patients and proxies.

The primary outcome of this study will be health-related quality of life over time as measured using the EQ-5D questionnaire. Secondary outcomes include health-related quality of life over time as measured using the SF-36 questionnaire, and differences in separate domains of both health-related quality of life questionnaires (EQ-5D and SF-36).

The researchers aim to recruit consenting adult patients (REVERSE only recruits adult patients) that acquire a CRE, CRPA, or CRAB hospital-acquired infection (main outcome of the RCT) during their hospital stay.

Mixed-effects models with optimal type of mixed-effects model (e.g. mixed-effects linear model or mixed-effects beta-regression) determined by model fit. Exposed patients (infected with organism of interest) and unexposed patients will be matched on ward, time in hospital before index date, and age (categorical: 18-44, 45-64, 65-74, 75+ years).

The analysis will include fixed effects for the matching variables and the following additional covariates: sex, comorbidities (Charlson Comorbidity Index), surgical procedure within 30 days before the index date (date of matching), antibiotic use within 30 days before the index date. Time will also be included as a covariate to model changes over time, with an interaction with the exposures of interest to model potential time-varying effects of the exposure. Total quality

of life losses will be estimated and compared by obtaining the area under the curves for exposed and unexposed groups using Simpson's rule (quadratic interpolation).

A cluster-specific and patient-specific random effect will be considered to model the repeated measurements on the same cluster and patient. Supportive analyses considering more complex random effects structures will also be investigated. (e.g., time within clusters, wards within hospitals). The interaction between time and interventions will also be added as a fixed effect to model a possible time-varying intervention effect.

It is possible that a limited number of individuals that are recruited as uninfected controls will attract a CRE/CRPA/CRAB infection at a later point during their hospitalisation. This is necessary to avoid bias introduced when selecting controls that will never be infected (conditioning on the future). In expectation, the number of people acquiring such infections is small and measurements on or after the day of infection in those patients originally assigned to the control group will be censored.

Intervention Type
Other

Primary outcome(s)
Health-related quality of life measured using the EQ-5D questionnaire at 0, 1, 3, 6, and 12 months

Key secondary outcome(s))
1. Health-related quality of life measured using the SF-36 questionnaire at 0, 1, 3, 6, and 12 months
2. Differences in separate domains of both health-related quality of life questionnaires (EQ-5D and SF-36) at 0, 1, 3, 6, and 12 months

Completion date
01/06/2026

Eligibility

Key inclusion criteria
1. Adult patient (≥18 years) admitted to a participating hospital on a participating ward
2. Able to speak/understand the local language or English well enough to fill out the surveys
3. Hospital-acquired infection caused by CRE/CRPA/CRAB or control from the same ward

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Unable to speak/understand one of the survey languages or English
2. Admitted to a ward or hospital not participating in REVERSE
3. Under 18 years of age
4. Admitted with infection caused by CRE/CRPA/CRAB (community-acquired infection)

Date of first enrolment
01/05/2022

Date of final enrolment
01/02/2026

Locations

Countries of recruitment
Greece

Italy

Romania

Spain

Study participating centre
Azienda Ospedaliera Universitaria Integrata Verona
Piazzale L.A. Scuro, 10
Verona
Italy
37134

Study participating centre
Policlinico Universitario A. Gemelli Rome
Via della Pineta Sacchetti 217
Rome
Italy
00168

Study participating centre
Policlinico S.Orsola Bologna
Via Giuseppe Massarenti 9

Bologna
Italy
40138

Study participating centre
ASST Santi Paolo e Carlo Milano
Via Antonio di Rudinì 8
Milan
Italy
20142

Study participating centre
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milano
Ospedale Maggiore Policlinico Milano
Via Francesco Sforza 35
Milan
Italy
20122

Study participating centre
Hospital Universitario Jerez de la Frontera
Ctra. Trebujena, s/n
Jerez de la Frontera
Spain
11407

Study participating centre
Hospital Universitario Reina Sofía
Av. Menendez Pidal, s/n
Cordoba
Spain
14004

Study participating centre
Hospital Universitario Son Espases
Carretera de Valldemossa 79
Palma
Spain
07120

Study participating centre
Hospital del Mar
Passeig Marítim de la Barceloneta 25, 29
Barcelona
Spain
08003

Study participating centre
Hospital General Universitario de Alicante
Pintor Baeza 11
Alicante
Spain
03010

Study participating centre
Hospital Álvaro Cunquiero
Estrada de Clara Campoamor 341
Vigo
Spain
36213

Study participating centre
Laiko General Hospital
Agiou Thoma 17
Athens
Greece
11527

Study participating centre
Ippokrateio General Hospital
Vasilissis Sofias 114
Athens
Greece
11527

Study participating centre
AHEPA University Hospital of Thessaloniki
Kiriakidi 1

Thessaloniki
Greece
54621

Study participating centre
University Hospital of Ioannina
Niarxou Avenue
Ioannina
Greece
45500

Study participating centre
Attikon General Hospital
Rimini 1
Chaidari
Greece
12462

Study participating centre
Military Hospital Bucharest
Calea Plevnei Nr. 134
Bucharest
Romania
010825

Study participating centre
University Emergency Hospital Bucharest
Splaiul Independenței 169
Bucharest
Romania
050098

Study participating centre
Timisoara Municipal Clinical Emergency Hospita
Strada Daliei Nr. 17
Timisoara
Romania
300254

Study participating centre
Targu Mures County Hospital
Str. Gh. Marinescu Nr. 1
Targu Mures
Romania
540103

Study participating centre
Sibiu County Emergency Hospital
Bulevardul Corneliu Coposu 2-4
Sibiu
Romania
550245

Study participating centre
Fundeni Hospital
Sos Fundeni Nr. 258, Sector 2
Bucharest
Romania
022328

Study participating centre
Sismanoglio General Hospital
Sismanogliou 37
Marousi
Greece
151 26

Sponsor information

Organisation
University of Zurich

ROR
https://ror.org/02crff812

Funder(s)

Funder type

Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
The following applies to persons outside of the REVERSE consortium. The data will be available after publication. The project email can be used to contact the coordinating team regarding data requests (reverse@usz.ch). Data will be made available where possible to support further research under FAIR principles, except for data that are confidential or cannot be shared under the GDPR regulations. De-identified and aggregate data from the cohort study needed to verify results will also be available for approximately 5 years after the project ends. Please note, participant-level data from the cohort study will not be available due to patient-level confidential information. The researchers will share data electronically with other research groups conducting meta-analyses or reviews on Infection Prevention and Control (IPC), Antibiotic Stewardship (ABS), or Microbiology and Diagnostic Stewardship (MDS) interventions. This adheres to the data-sharing rules outlined in the Grant Agreement with the European Commission.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participants version 1.1	14/03/2022	16/03/2022	No	Yes
Participant information sheet	Representatives version 1.1	14/03/2022	16/03/2022	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 1.2	14/03/2022	16/03/2022	No	No
Protocol file	version 1.4	01/06/2023	05/02/2024	No	No

Statistical Analysis Plan			09/04/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes