

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

<b>Submission date</b> 16/03/2022	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 21/03/2022	<b>Overall study status</b> Ongoing	<input checked="" type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 09/04/2024	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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 questionnaires 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

**Study website**  
<http://www.reverseproject.eu/>

## Contact information

**Type(s)**  
Scientific

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### **Type(s)**

Principal Investigator

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## **Additional identifiers**

### **EudraCT/CTIS number**

Nil known

### **IRAS number**

### **ClinicalTrials.gov number**

Nil known

### **Secondary identifying numbers**

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

### **Secondary study design**

Cohort study

### **Study setting(s)**

Hospital

### **Study type(s)**

Quality of life

### **Participant information sheet**

See additional files

### **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 measure**

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

## **Secondary outcome measures**

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

## **Overall study start date**

01/07/2021

## **Completion date**

01/06/2026

# **Eligibility**

## **Key inclusion criteria**

1. Adult patient ( $\geq 18$  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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

4500

**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  
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03010

**Study participating centre**  
**Hospital Álvaro Cunqueiro**  
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

**Sponsor details**

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**Sponsor type**

University/education

**Website**

[http://www.uzh.ch/index\\_en.html](http://www.uzh.ch/index_en.html)

**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, Ευρωπαϊκή Επιτροπή, Европейская комиссия, Evropské komise, Commission européenne, Choimisiúin Eorpaigh, Europskoj komisiji, Commissione europea, La Commissione europea, Eiropas Komisiju, Europos Komisijos, Európai Bizottságrol, Europese Commissie, Komisja Europejska, Comissão Europeia, Comisia Europeană, Európskej komisii, Evropski komisiji, Euroopan komission, Europeiska kommissionen, EC, EU

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location****Results and Publications**

**Publication and dissemination plan**

- 1. Results will be published in peer-reviewed journals with open access policies where possible.
- 2. Periodic reports will be distributed to stakeholders and the funding agency
- 3. Aggregate data will be available upon request

**Intention to publish date**

30/01/2027

**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?
<a href="#">Participant information sheet</a>	Participants version 1.1	14/03/2022	16/03/2022	No	Yes
<a href="#">Participant information sheet</a>	Representatives version 1.1	14/03/2022	16/03/2022	No	Yes
<a href="#">Protocol file</a>	version 1.2	14/03/2022	16/03/2022	No	No
<a href="#">Protocol file</a>	version 1.4	01/06/2023	05/02/2024	No	No
<a href="#">Statistical Analysis Plan</a>			09/04/2024	No	No