# WP6 Replication Study: The risk of acute liver injury associated with the use of antibiotics: Population based case control study

**First published:** 05/09/2012

**Last updated:** 29/10/2013

Study Ongoing

## Administrative details

**EU PAS number**

EUPAS2946

**Study ID**

5053

**DARWIN EU® study**

No

**Study countries**

United Kingdom

**Study description**

This study builds on previous work within the EU-PROTECT Programme (http://www.imi-protect.eu/), that examined different methodological approaches to pharmacoepidemiological research design to investigate, by using a case study of antibiotic induced liver injury, the population case control approach. The study proposes to replicate a previous analysis, to ensure that the baseline model is identical, and then perform sensitivity analyses to understand how changes to input parameters (such as definition of current exposure, code selection, definition of outcome and study periods) may affect the estimates of risk of acute liver injury associated with antibiotics in the general population.The analyses will be performed using the UK General Practice Research Database (CPRD /GPRD). The study design is a population based case control study, with definite and possible cases defined using an algorithm that incorporates consultation diagnosis codes, referral to specialist codes and liver laboratory analyses.Conditional logistic regression is used to analyse the matched data.

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**Study status**

Ongoing

# Research institutions and networks

## Institutions

### Takeda

**First published:** 01/02/2024

**Last updated:** 01/02/2024

**Institution**

# Networks

## PROTECT

- Belgium
- Denmark
- France
- Germany
- Italy
- Netherlands
- Poland
- Spain
- Sweden
- Switzerland
- United Kingdom

**First published:** 26/06/2013

**Last updated:** 14/01/2025

Network

# Contact details

**Study institution contact**

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Study contact

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**Primary lead investigator**

David Irvine

**Primary lead investigator**

## Study timelines

**Date when funding contract was signed**
Planned: 01/02/2011

Actual: 01/02/2011

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**Study start date**
Planned: 13/11/2012

Actual: 04/12/2012

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**Data analysis start date**
Planned: 08/01/2013

Actual: 08/01/2013

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**Date of final study report**
Planned: 12/12/2013

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Takeda Development Centre (Europe)

## Regulatory

**Was the study required by a regulatory body?**

No

# Methodological aspects

## Study type

## Study type list

**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

Other

**If ‘other’, further details on the scope of the study**

Replication of previous anlysis in the same database, followed by sensitivity analyses

**Main study objective:**

The main objective is to replicate a previous analysis of data in the same database, blinded to the results, under the same work programme (http://www.imi-protect.eu/) . This will be followed by an examination of the robustness of the strength of the association, altering a variety of parameters. Validation of Acute Liver Injury may be sought through a GP questionnaire.

## Study Design

**Non-interventional study design**

Case-control

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(J01) ANTIBACTERIALS FOR SYSTEMIC USE

ANTIBACTERIALS FOR SYSTEMIC USE

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**Medical condition to be studied**

Liver injury

## Population studied

**Age groups**

- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)
- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

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**Estimated number of subjects**

12000

## Study design details

**Outcomes**

To estimate the relative risk of acute liver injury associated with antibiotics exposure (users vs. non-users).To estimate the relative risk of acute liver injury comparing various antibiotics classes.To estimate the relative risk of acute liver injury comparing specific individual antibiotics. A questionnaire to GP may seek validation of the computerised diagnosis. To assess the effect of dose and duration of use for specific individual antibiotics.Various definitions of exposure time, recovery time, and criteria for inclusion of confounders/ effect modifiers will be will be altered to examine the robustness of the association.

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**Data analysis plan**

The population based case control study will be analysed by conditional logistic regression. Matching will be on age at birth, gender and Practice. Odds ratios and 95% confidence intervals will be computed to examine the association between first occurrence of idiopathic acute liver injury and exposure to antibiotics (as a group, in different classes (tetracycline, penicillins & betalactamic, cephalosporin, macrolides, aminoglycosides, quinolones and other antibiotics and combinations), and individual drugs where possible).A series of bivariate models will be examined to evaluate the contribution of confounder / effect modification variables. Stepwise inclusion methods will be used to improve model fit evaluated by the Likelihood Ratio test. A full model with all such variables will be constructed.These procedures will be repeated in sensitivity analyses, changing exposure window length, definitions for case inclusion, and extending the length of liver injury recovery time.

## Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

**Data source(s)**

Clinical Practice Research Datalink

**Data source(s), other**

CPRD

**Data sources (types)**

Electronic healthcare records (EHR)

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Unknown

**Check completeness**

Unknown

**Check stability**

Unknown

**Check logical consistency**

Unknown

# Data characterisation

**Data characterisation conducted**

No