

# Delayed care in breast cancer patients Case study report Use case B, Deliverable 6.2, 03.06.2022

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## 1. Executive summary

In this report, we present the development of a research question focused on exploring whether the COVID19 pandemic, because of both the epidemiological situation and the public health measures imposed on the population, changed existing patterns of non-COVID-19 health care utilisation; in particular, we have studied any variation in the delay from breast cancer diagnosis to first treatment. We have also analysed whether these changes affected differently to different populations within and between countries or regions.

Healthcare systems all across Europe have had to reorganize services and reallocate resources to provide attention to COVID-19 patients. Because of the increase of cases that required intensive attention or because of the inherent risk of COVID-19 nosocomial infection, all countries have been forced to cancel or postpone non-urgent care (e.g., elective surgery). Preliminary and local evidence suggests that essential elective care including cancer treatments endured delays.

In this study, a cohort of women, 18 years old or older, with a first diagnosis of breast cancer between January 2017 and December 2021, based on individual level health record, and administrative data, were analysed in several countries and regions in Europe. Using the PHIRI privacy-preserving federated approach, data hub computed statistical analyses on the monthly distribution of the times between the breast cancer diagnosis and a series of possible first line treatments (i.e. surgery, radiotherapy, hormonotherapy, immunotherapy and chemotherapy).

We have shown that countries and regions' figures with regard to delays in time-to-firsttreatment associated with the COVID-19 crisis in women with breast cancer have been observed to be heterogeneous.

This report also offers some recommendations and key points in population health research using a federated approach.

### 2. Key points

We have discovered differences in time-to-treatments across countries in the impact of the COVID-19 lockdown and subsequent months.

The deployment of this use case has been feasible in a variety of nodes (both national and regional nodes); however, there is a learning curve both in the understanding of the federated approach and in the deployment of the technologies.

Uneven IT capacity and lack of a clear view of the task has implied some delays that have been fine-tuned while doing. The main effort resides in the access to data.

Those premises with IT capacity and easy access to data are likely to comply with the whole pipeline with an affordable cost.

We have to wait for the rest of the interested nodes to assess any other difficulty not revealed in this group of nodes.



## PHIRI: Case study report. Use case B

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## I. Introduction

Healthcare systems across Europe reorganized services and reallocated resources to provide attention to COVID-19 patients. Because of the rampant increase of cases that required intensive attention or because of the inherent risk of COVID-19 infection, all countries have been forced to cancel or postpone non-urgent care (e.g., elective surgery). Preliminary and local evidence suggests the presence of delayed care in cancer diagnosis and optimal treatments. However, the uneven intensity of restriction measures along the pandemic may have had a different impact in treatment delays.

The objective of this use case is to study in women with breast cancer whether there have been delays in accessing breast cancer treatments (chemotherapy, surgery, radiotherapy, etc. ...) as a consequence of the stringency measures implemented to control the COVD19 pandemic.

## II. Approach

#### A. General approach

Use case B followed the PHIRI federated pipeline (see image). In this case, the PHIRI orchestrating node (IACS) is acting as both orchestrator and promoter of the use case.



#### Orchestration of research query sent out to the federation

Figure 1 Federated analysis pipeline



### B. Methodology for this specific use case

#### Study design

Quasi-experimental pre-post study with a historical control that is the same population base analysed before an empirical joint point.

This joint point, the equivalent to the exposure, will be the first joint point after Dec 31<sup>st</sup>, empirically estimated upon the deseasonalized trend in "monthly time-to-treatment" observations since the inception of the cohorts.

The main endpoint is the change in time-to-treatment before and after the joint-point. Breast cancer treatments to analyse will be elective surgery, radiotherapy, hormonal therapy or chemotherapy.

#### Description of the study population

Virtually the universe of breast cancer patients treated in the participant regions since January 2017 (until December 2021). Looking backward in time will enable us to set a proper baseline for the analyses to detect change in time-to-treatments, if it exists.

#### Variables

In the following link it can be accessed the data model that is common to the participating nodes: <u>https://doi.org/10.5281/zenodo.5148021</u>

#### Methods, data processing and analysis

#### Data processing

The data extraction will follow the model proposed here <u>https://doi.org/10.1186/s13690-021-00731-z</u>. In essence, this pipeline starts with a decision on the common data model where participating nodes agree on those variables essential to the research query, realize on the actual availability of the required data, and agree on semantics crosswalks across the different encoding systems in place. Participant nodes will link their data sources if needed, retrieve the data and transform them to fit into the common data model.

All the data mobilization, analyses and results devolution will follow the pipeline depicted in the figure above (*Figure 1*), as part of the client-server federation implemented in PHIRI where the coordination hub will be in charge of the orchestration of the federation of data hubs.

This entire pipeline is contained in a Docker solution provided by the coordination hub (as here <u>https://doi.org/10.5281/zenodo.5729310</u>) that will act as a secure processing environment.

#### Data quality

The basis for the quality control is the development of a common data model (ensuring semantic interoperability across nodes) and the implementation of an *ad hoc* quality assessment analysis contained in the Docker image. As here <u>https://doi.org/10.5281/zenodo.6717381</u> (see DQA interactive reports).



#### Data analyses

Data analytics are contained in the Docker image. The pipeline includes a descriptive analysis on both monthly surgical and medical treatments, and median-monthly time-spams to treatment over the study period will be carried out. As here <u>10.5281/zenodo.6717381</u> (see local interactive reports by region, country).

### III. Results

#### Participating nodes and level of progress

Four nodes have completed the deployment of the analytical pipeline in their premises (Belgium (BE), Wales (UK), Marche (IT), and Aragon (ES)). Others are ongoing; so, Latvia is fixing some errors in their dataset while writing this report; in turn, Croatia, Estonia and Slovenia showed availability for the deployment of the use case.

Data quality analysis provides information on the missing data, anomalous distributions, impossible values, and information gaps. This is the summary provided by the data quality assessment script applied to a preliminary dataset from Latvia:

verview Alerts 14 Reproduction	
lerts	
country_cd has constant value "LV"	Constant
time_dx_to_immunotherapy_nm has constant value "1035.0"	Constant
<pre>socecon_lvl_cd has 2983 (100.0%) missing values</pre>	Missing
country_origin_cd has 2983 (100.0%) missing values	Missing
time_dx_to_surgery_nm has 117 (3.9%) missing values	Missing
time_dx_to_radiotherapy_nm has 1654 (55.4%) missing values	Missing
time_dx_to_chemotherapy_nm has 2074 (69.5%) missing values	Missing
time_dx_to_immunotherapy_nm has 2982 (> 99.9%) missing values	Missing
time_dx_to_hormonotherapy_nm has 2694 (90.3%) missing values	Missing
patient_id has unique values	Unique
socecon_lvl_cd is an unsupported type, check if it needs cleaning or further analysis	Unsupported
country_origin_cd is an unsupported type, check if it needs cleaning or further analysis	Unsupported
time_dx_to_surgery_nm has 1167 (39.1%) zeros	Zeros
time_dx_to_chemotherapy_nm has 76 (2.5%) zeros	Zeros

#### Actual results

The main results of the local analyses show for each country the monthly evolution of breast cancer cases as diagnosed by the healthcare system (*Figure 2*), and the evolution of the median time (in days) from breast cancer diagnosis to first treatment, being it: surgery (*Figure 3*), radiotherapy (*Figure 4*) or chemotherapy (*Figure 5*).

We fitted a local weighted smoothing (*loess*) regression to each trend as a non-parametric smoothing technique to reveal trends and cycles in data, that might be difficult to model with a parametric curve. In addition, we marked March 2020 with a dotted vertical red line to facilitate the identification of changes in the trend after the start of the pandemic and the implementation of public health measures.









#### Figure 3. Evolution of time from breast cancer diagnosis to surgery as first treatment



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#### Figure 4. Evolution of time from breast cancer to radiotherapy as first treatment





Download the interactive HTML local reports with complete results here: <u>https://doi.org/10.5281/zenodo.6717381</u>



## **IV. Implications and limitations**

#### Level of maturity

The federated approach had been tested elsewhere [1] which has facilitate the design, implementation and deployment of the use case.

#### Issues to improve future deployments

As a consequence of the implementation and deployment of the use case, a number of issues have been detected:

- IT capacity across nodes is uneven; setting up a help desk has allowed reducing the risks of lack of compliance, particularly solving deployment issues and patching errors in the pipeline.
- Having Data Protection Offices-DPO's involved in the process improves the understanding of the Docker solution as a secure environment in terms of GDPR.
- Using an asynchronous approach allows front-runners to get the results as soon as they access the data, while others join after solving implementation and deployment issues.
- A disclosure policy is needed when it comes to the publication and sharing of the HTML reports and aggregated data tables. Dropping outlier values in the graphs and truncate cells with less than five cases is advisable.



## V. Conclusions and recommendations

Differences in time-to-treatment across countries in the impact of the COVID19 lockdown and subsequent months have been discovered.

The deployment of this use case has been feasible in a variety of nodes; however, there is a learning curve both in the understanding of the federated approach and in the deployment of the technologies.

Uneven IT capacity and lack of a clear view of the task has implied some delays that have been fine-tuned while doing. The main effort resides in the access to data.

Those premises with IT capacity and easy access to data are likely to comply with the whole pipeline with an affordable cost.

To wait for the rest of the interested nodes to assess any other difficulty not revealed in this group of nodes, is needed.



## 3. References

- González-García, J., Estupiñán-Romero, F., Tellería-Orriols, C. et al. Coping with interoperability in the development of a federated research infrastructure: achievements, challenges and recommendations from the JA-InfAct. Arch Public Health 79, 221 (2021). <u>https://doi.org/10.1186/s13690-021-00731-z</u>
- 2. Enrique Bernal-Delgado, & Marc Van den Bulcke. (2022). PHIRI WP6 Use Case B Common Data Model (2.0.0). Zenodo. <u>https://doi.org/10.5281/zenodo.6357891</u>
- Francisco Estupiñán-Romero, Javier González-Galindo, Natalia Martínez-Lizaga, & Enrique Bernal-Delgado. (2022). PHIRI - WP6 - Use Case B scripts for local analyses (R Markdown) (4.0.0). Zenodo. <u>https://doi.org/10.5281/zenodo.6359893</u>
- Javier González-Galindo, Francisco Estupiñán-Romero, David Chichell-Ruíz, Juan González-García, Carlos Tellería-Orriols, & Enrique Bernal-Delgado. (2022). PHIRI APP - WP7 - PHIRI Federated Research Infrastructure (FRI) - D7.1 Small-scale prototype of PHIRI federated infrastructure (2.2.2). Zenodo. <u>https://doi.org/10.5281/zenodo.6483177</u>



## 4. Disclaimer

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