PHIRI
Population Health Information Research Infrastructure

PHIRI Use Cases –measuring the impact of COVID-19 on population health

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ROBERT KOCH INSTITUT

IACS Instituto Aragonés de Ciencias de la Salud

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101018317

Research Use Cases on COVID-19 – Objectives

4 real life research use cases measuring the impact of COVID-19 on population health

- Direct and indirect determinants of COVID-19 infection and outcomes in vulnerable population groups with reference to inequalities
- COVID-19 related delayed care in breast cancer patients
- The impact of COVID-19 on perinatal health and perinatal health inequalities
- COVID-19 related changes in population mental health

Demonstrate how a broad variety of data (e.g. administrative and survey data) can be reused in a distributed way across Europe:

a) **Conduct research** through use cases of immediate relevance on the consequences of the COVID-19 pandemic on European population health

b) **Pilot activities** for the benefits and added value of a federated research infrastructure by bringing together data from different European countries

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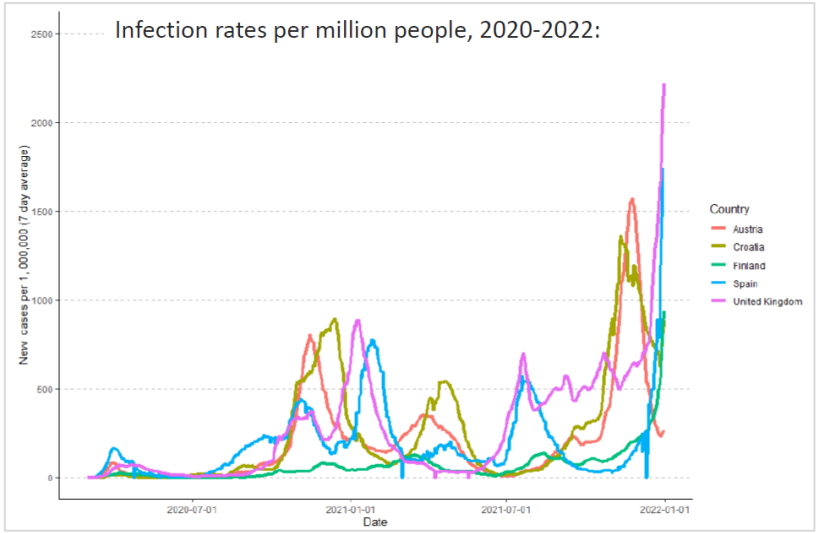
Research Use Cases on COVID-19 – Results

Has the COVID19 pandemic changed existing patterns of non-COVID-19 health care utilisation for (vulnerable) populations within and between countries?

- Heart attack and strokes (Cohort 1)
- Hip and knee replacements (Cohort 2)
- Serious trauma admissions (Cohort 3)

	Associated entity in ERD	Label (var_label)	Name (var_concept)	Classification/Encoding	Units	Format	Description
basics	patient	**patient_id**	patient identificator	private key ciphering function	none	string	patient pseudonymized identificator
	patient	**sex**	sex				
	patient	**age_nm**	age	none	years	integer	patient's age as of 2019-01-01
	observation period	**period**	[time period]	none	month	integer	natural month
cohort 1	heart event	**acute_event_heart**	major vascular event - heart attack	ICD10:I21			
	date heart event	**date_event_heart**	date - heart attack	date	date_DMY_nr	YYYY-mm-dd	
	stroke event	**acute_event_stroke**	major vascular event - stroke	I60-I64			
	date stroke event	**date_event_stroke**	date - stroke		date_DMY_nr	YYYY-mm-dd	
cohort 2	procedure	**ttm_type_cd**	type of treatment	types of treatment referred	none	integer	type of treatment received by the patient
	procedure	**surgery_elective_hip**	elective surgery, hip joint replacement	OPCS codes in UK W37-W39			
	procedure	**surgery_elective_knee**	elective surgery, knee joint replacement	OPCS codes in UK W40-W42			
cohort 3	condition	**acute_event_trauma**	hospital admission for trauma based on	ICD10: S720, S721, S722, S723,	none	string	Based on scientific analysis by New
	Date of event	**date_event**	date of admission	date	date_DMY_nr	YYYY-mm-dd	date of admission
	Optional:						
optional	patient	**educ_cd**	highest completed education level	quintile or top/bottom	quintiles	integer	patient's highest completed education
	patient	**socecon_lvl_cd**	socioeconomic level	quintile or top/bottom	quintiles	integer	patient's socioeconomic level (quintile)
	patient	**country_cd**	country (residence)	ISO3166	none	string	patient's country of residence
	patient	**district_cd**	district (residence)	e.g. Eurostat NUTS			
	patient	**country_origin_cd**	country (origin)	ISO3166	none	string	patients' country of origin (country of



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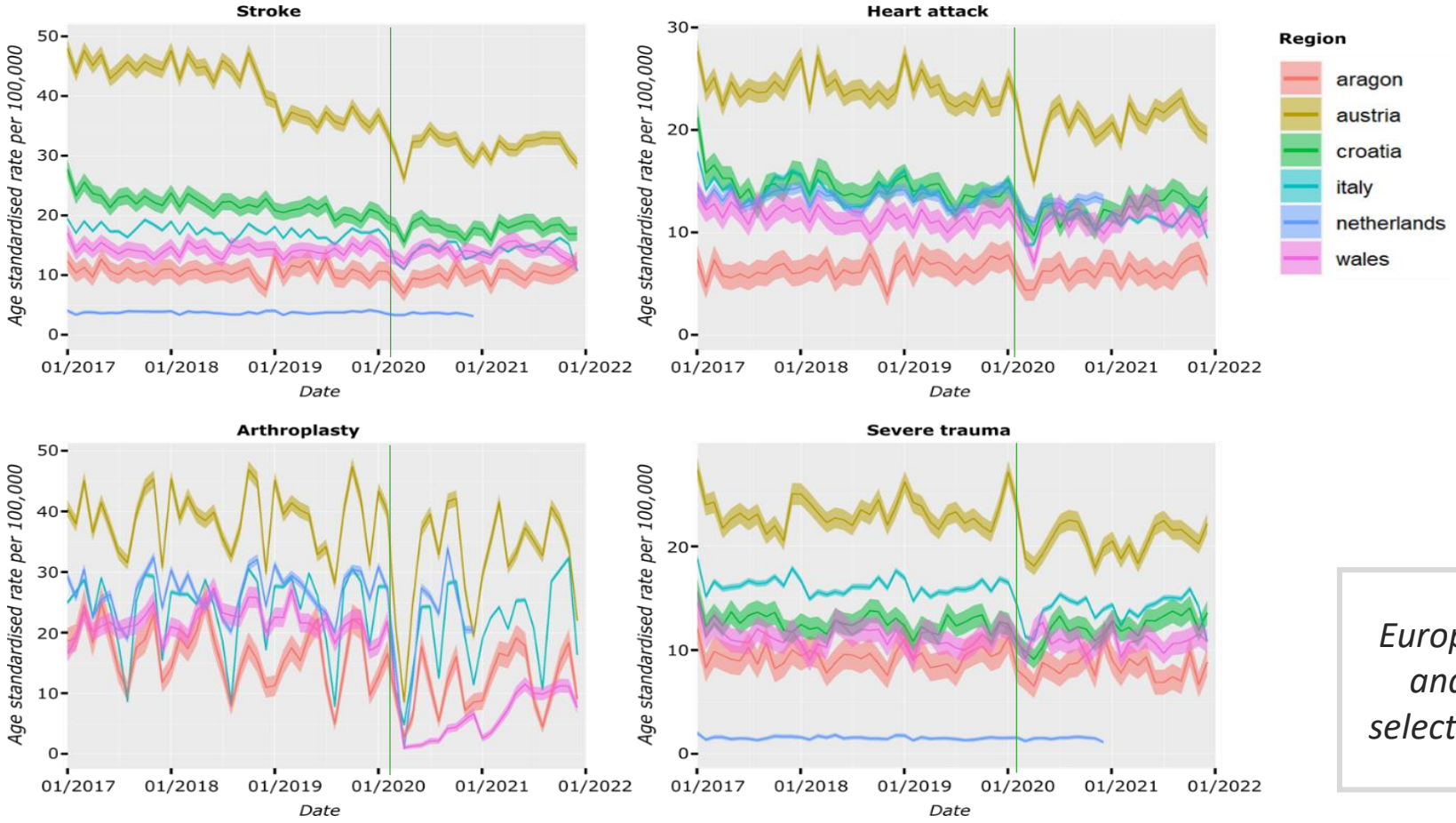
Research Use Cases on COVID-19 – Results



European age-standardised rates (solid lines) and the 95% CI (shaded area) across four selected forms of HCU in six European regions.

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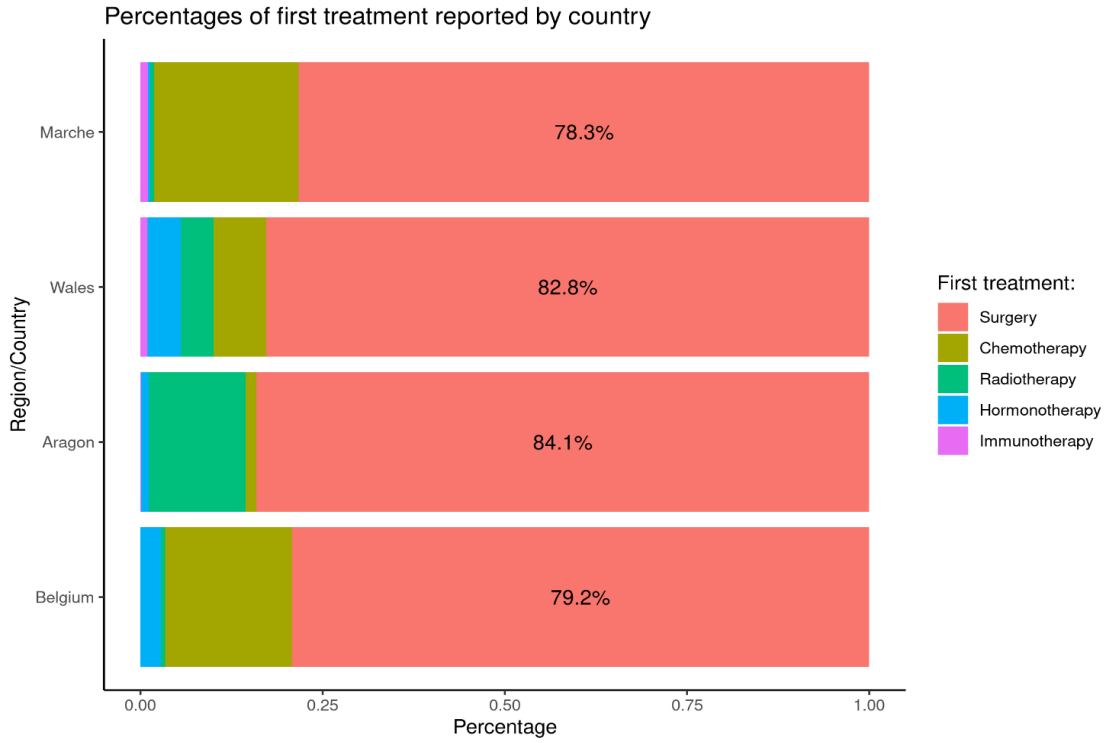
Research Use Cases on COVID-19 – Results

Was there any delay in the treatment of breast cancer patients associated with the COVID-19 pandemic?

Data hubs participation: N = 4

Aragon (AR, Spain), Wales (WA, United Kingdom), Belgium (BE), Marche (MA, Italy)



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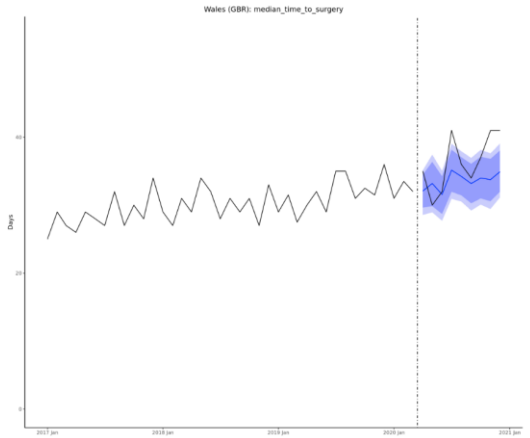
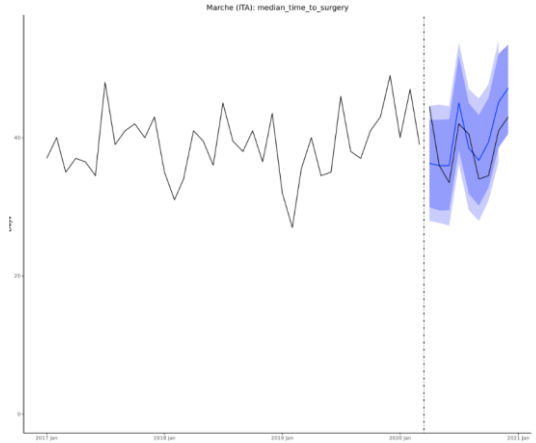
Research Use Cases on COVID-19 – Results

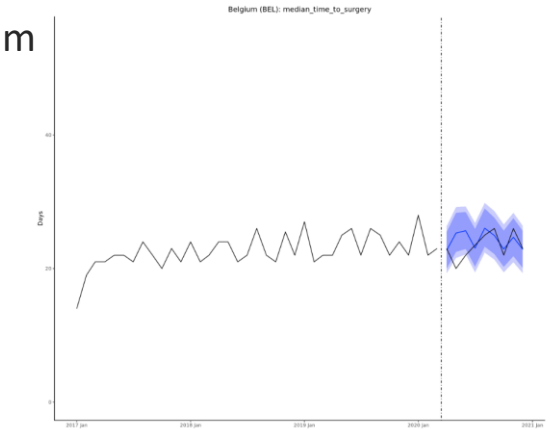
Wales



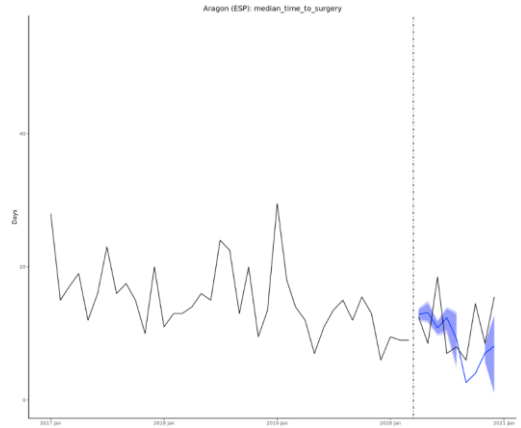
Marche, IT



Belgium



Aragon, ES



Forecast, 39 observations, NN

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Research Use Cases on COVID-19 – Results

Were population indicators of maternal and newborn health affected by the pandemic/lockdown?

Stillbirth (baby born without signs of life)

- 3-4 per 1000 births (15-18,000 babies per year in Europe)
- High health and psychological burden for parents, costs for families and society

Preterm birth (birth before 37 weeks of gestation)

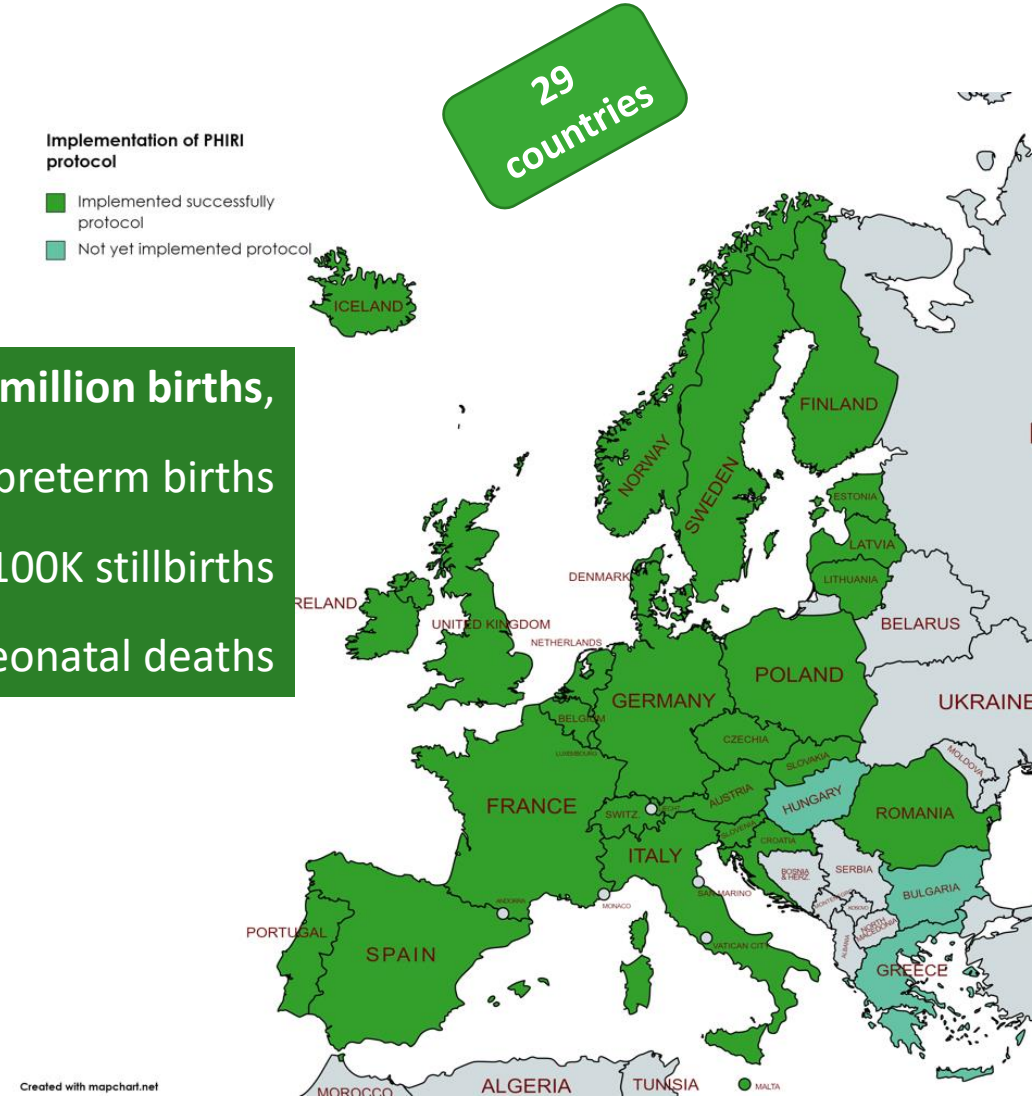
- Affects about 350,000 births per year in Europe, few effective prevention strategies
- Principal cause of infant death
- Long-term neurodevelopment impairment and other health problems among survivors

>29 million births,

>2M preterm births

100K stillbirths

37K neonatal deaths



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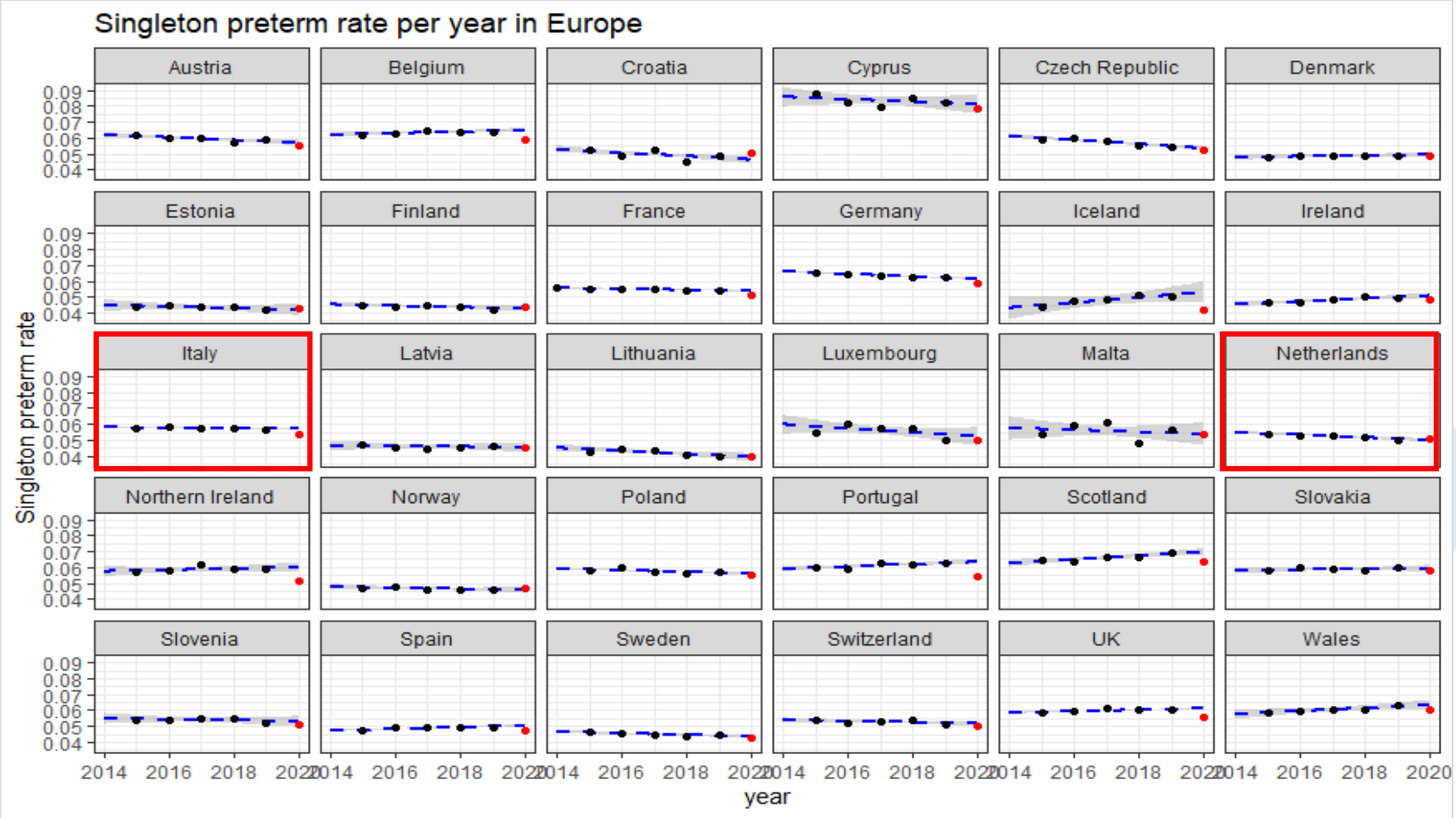
Research Use Cases on COVID-19 – Results



Pooled estimate
RR=0.96 (0.96 to 0.98) = 4% decrease in preterm birth

High heterogeneity
I^2 = 77.5% (proportion of total variation in effect estimate due to between-study heterogeneity)

Range of effects = 10% decrease in preterm birth to moderate increase of 3 to 4%.

Countries with stronger effects: Portugal – Belgium – UK – Spain – Italy – France

Countries with no effects: Nordic and Baltic countries, Netherlands

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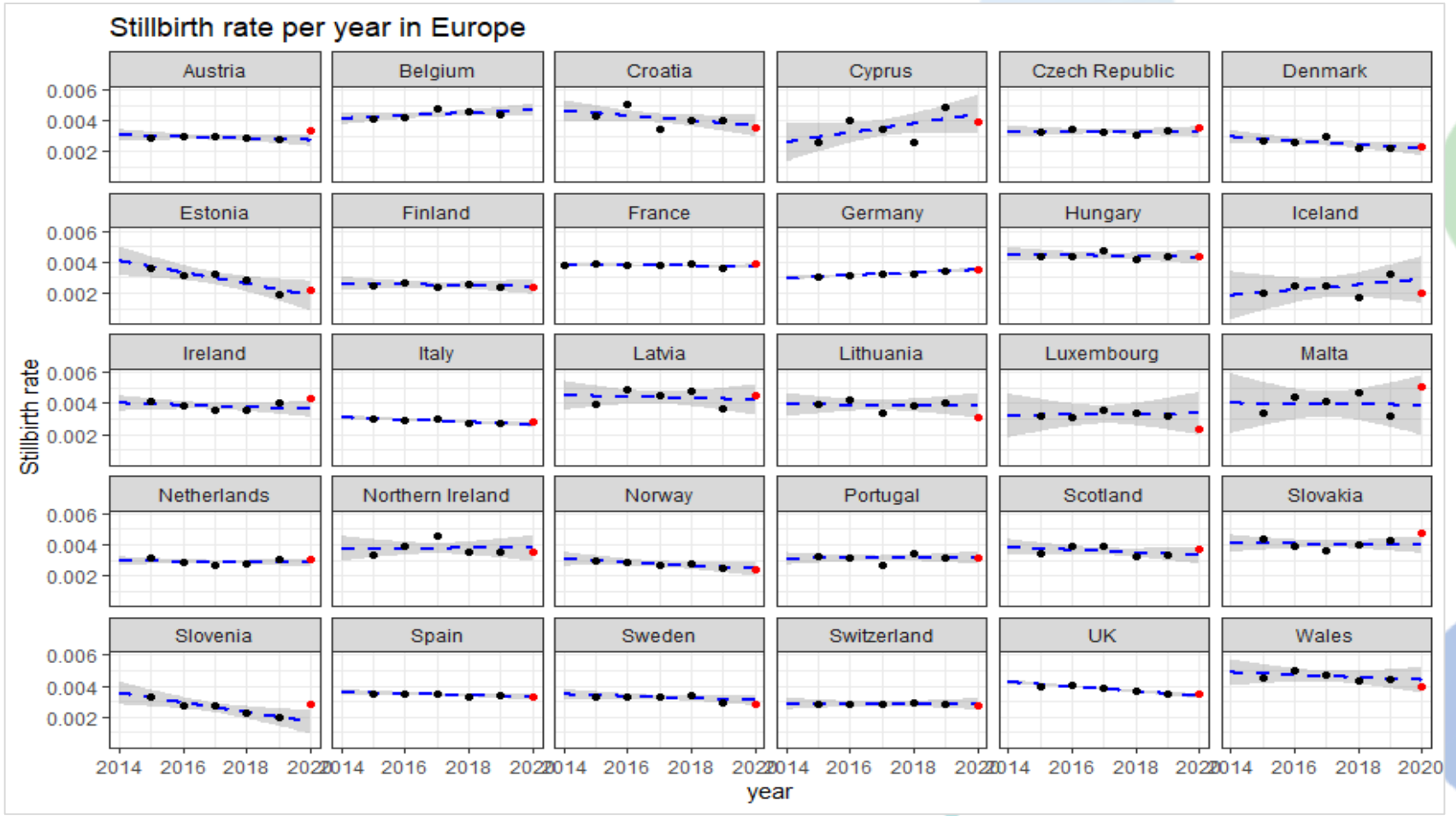
Research Use Cases on COVID-19 – Results

Estimate of pooled effect
RR=1.05 (1.02 to 1.08) = 5% increase in stillbirth

Lower heterogeneity
I^2 = 20.3% (proportion of total variation in effect estimate due to between-study heterogeneity)

Range of effects = No decreases significant / Austria higher stillbirth rates



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Research Use Cases on COVID-19 – Results

Has the mental health status (depression/anxiety) of the general population changed during the COVID-19 pandemic?

Table 3: Proportion of respondents reporting having negative feelings by age and gender, EU27 (%)

		Summer 2020			Spring 2021		
		Tense	Lonely	Depressed	Tense	Lonely	Depressed
Men	18–34 years	34	25	21	46	35	34
	35–49 years	30	21	19	41	31	32
	50+ years	22	18	15	28	26	23
Women	18–34 years	45	30	28	52	38	40
	35–49 years	38	22	27	49	34	39
	50+ years	24	18	17	35	30	29

Notes: *Green = lowest value, red = highest value. All differences between the two time periods are statistically significant. Any discrepancies between the figures in the text and table are due to rounding.*

Source: Living, working and COVID-19 e-survey data. Mental health and trust decline across EU as pandemic enters another year. EuroFound, 2021.

Results from 7 data hubs:

- Aragon (IACS)
- Austria
- Croatia
- Estonia
- Finland
- Romania
- Wales

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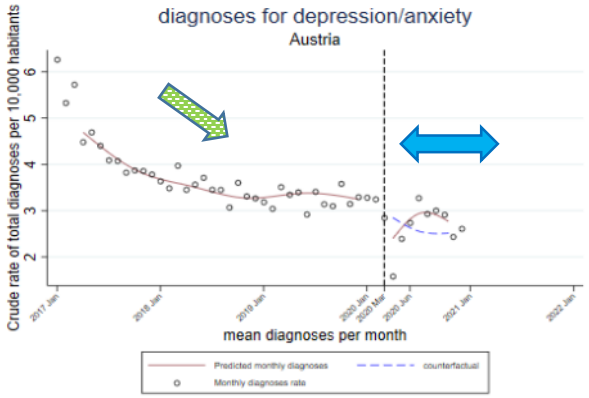
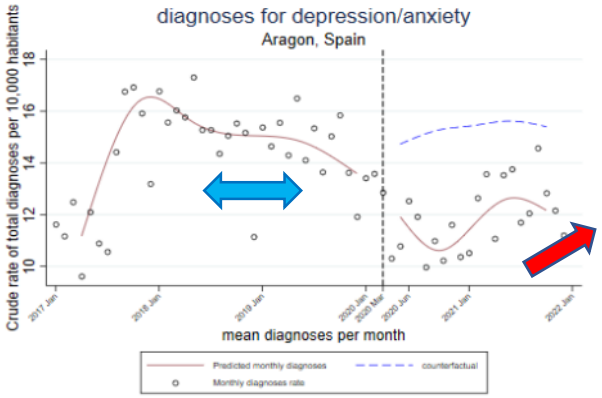
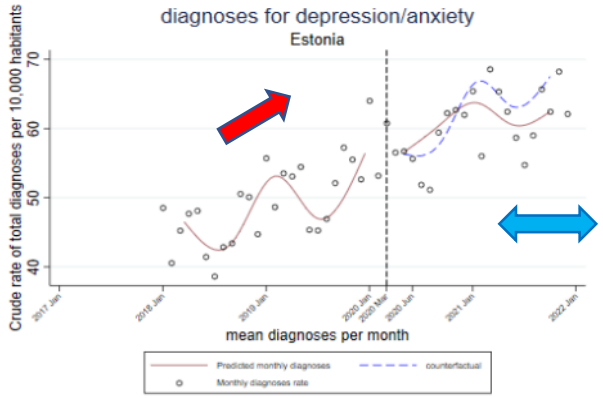
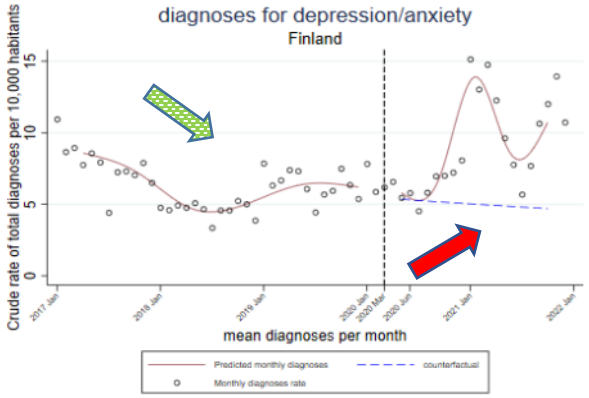
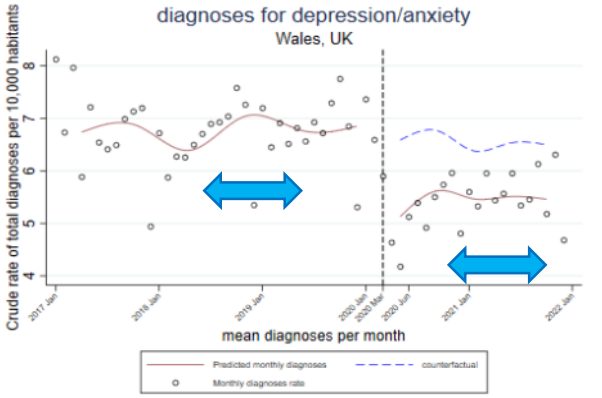
Diagnoses of depression or anxiety

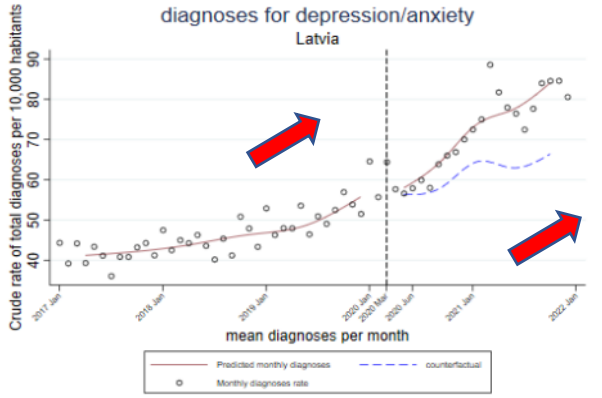


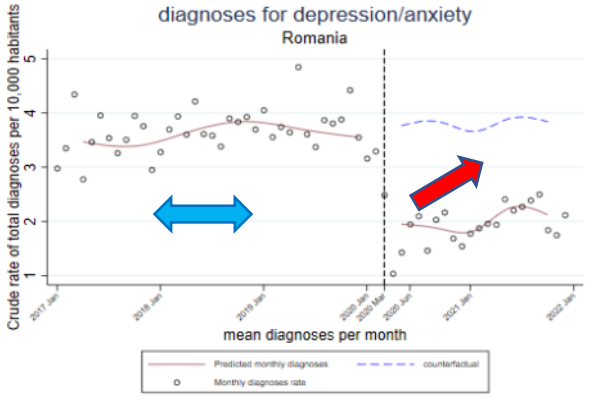












Decreasing trend

Increasing trend

Stable trend

Research Use Cases on COVID-19 – Achievements

Help desk supported use case deployment by ***45 Tickets, 278 Emails and 27 Meetings***

In ***14 data hubs****, the PHIRI-app Docker is already deployed and tested*

13 published releases *of PHIRI WP6 and WP7 on ZENODO*

In ***15 data hubs****, data is mobilized and (ready to be) analyzed in a distributed manner*

Special Issue in the European Journal of Public Health

PHIRI
Population Health Information Research Infrastructure

What do population health researchers need to reuse sensitive individual level data? How can the PHIRI federated approach help?

Enrique Bernal-Delgado, IACS, ES
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DIPoH
Distributed Infrastructure on Population Health

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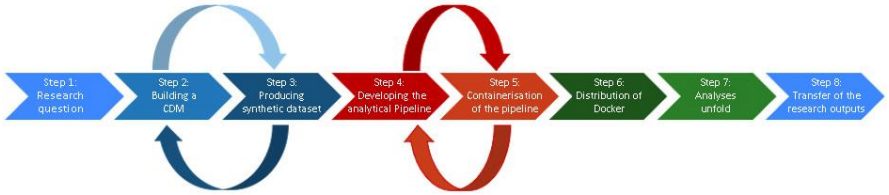
The issue

… when reusing data, particularly RWD, from multiple sites and multiple datasets

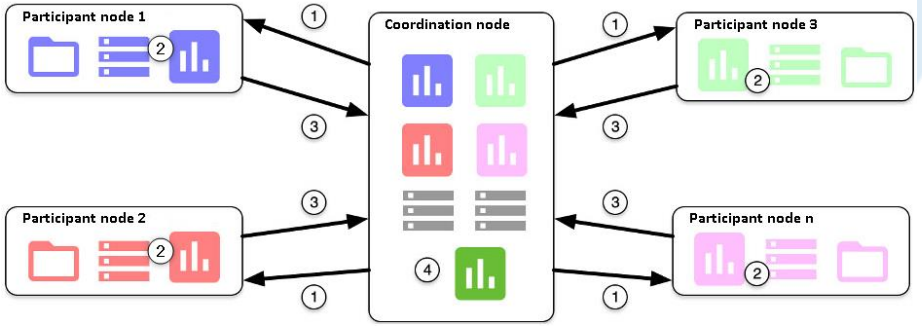
- Uneven data management capacity
- Poor harmonisation in data collection
- Poor standardisation in curation
- Poor datasets integration
- Quality issues in reuse
- Legal & ethical requisites – purpose, minimisation
- DPO sensitivity – risk aversion to reuse
- Uneven technical skills

The approach

- Data-visiting principle – “code meets data”
- Strict methodological workflow (LOST)



- Computational architecture

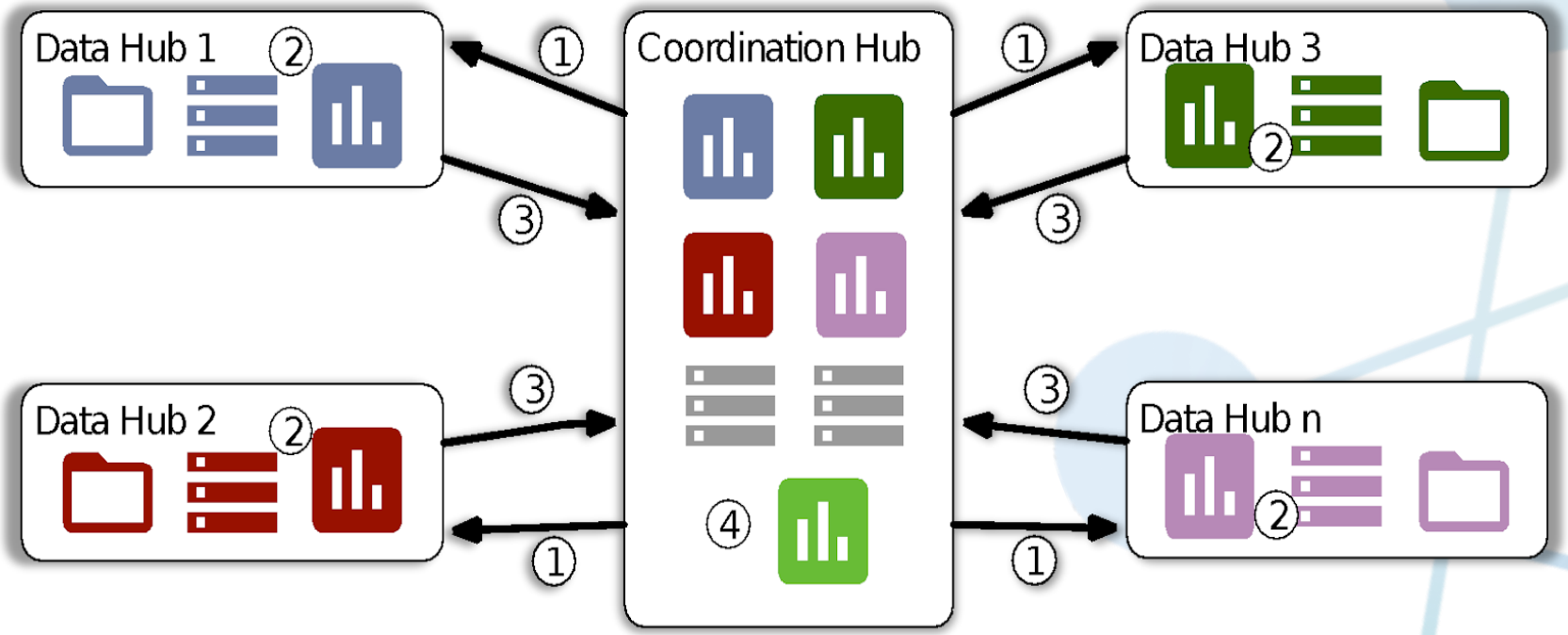


The principles

- **Research Question**
- **Secondary use**
- **Sensitive Health Data**
- Common Data Model (**CDM**)
- Security & **privacy by design**
- Enabling **rapid-cycle** analyses
- Aligned with HealthData@EU

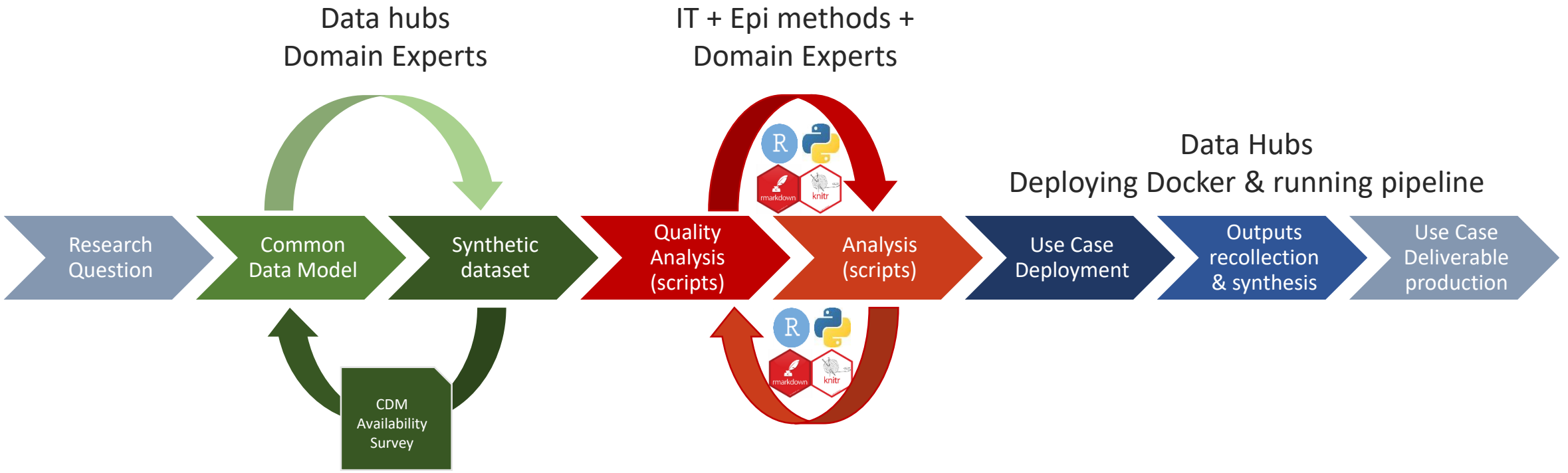
- **Federated**
- **Open source** (software/stack)
- **FAIR (stemming from R to F)**
- **Literate** statistical **programming**
- **Usability** (easy-to-use interfaces)
- Aligned with advances towards **Federated Learning**

Federated architecture



Federated, secondary use, “codes meets data” strong reliance on interoperability

Strict workflow enabling LOST interoperability



Common data model

PHIRI Federated Analysis Application (Docker)

- Common Data Model
- Synthetic dataset
- Quality Analysis (scripts)
- Analysis (scripts)
- Outputs recollection & synthesis

Data model entity	Variable							Data Quality	ETL	
Associated entity in ERD	Label (var_label)	Name (var_concept)	Level (required/recommended/optional)	Classification/Encoding	Units	Format	Description	References to validation rules	Transformation at or	
patient	**patient_id**	patient identificator	required	private key ciphering function	none	string	patient pseudonymized identificator	SHA256	double hash function a following SHA256 proto (see patient cohort defi in next sheet)	
patient	**age_nm**	age	required	none	years	integer	patient's age at the moment	3-digits; min 18; max 80	it might need to be calc from "birth_dt"	
patient	**socecon_lvl_cd**	socioeconomic level	recommended	quintile	quintiles	integer	patient's socioeconomic level (quintile)	min 1; max 5	it might need to be calc from "income_lvl" or approximated through combination of 'education_lvl" and othe variables	
patient	**country_cd**	country (residence)	required	ISO3166	none	string	patient's country of residence	ISO3166-3	conformance with ISO3166-3	field calculated at individual level
patient	**country_origin_cd**	country (origin)	recommended	ISO3166	none	string	patients' country of origin	ISO3166-3	conformance with ISO3166-3	field calculated at individual level
procedure	**ttm_type_cd**	type of treatment	required	types of treatment referred below or a combination of them	none	integer	type of treatment received by the patient	values restricted to existing categories	calculated following treatment type definition (see definitions in next sheets)	field calculated at individual level
procedure	**time_dx_to_surgery_nm**	[time til first surgery]	required	none	days	double	time from breast cancer diagnosis to first surgical procedure	no negative values allowed	it might be calculated as the difference between the date of the breast cancer diagnosis and the first surgical procedure related to the breast cancer treatment (see definitions in next sheets)	field calculated at individual level
procedure	**time_dx_to_radiotherapy_nm**	[time til first radiotherapy session]	required	none	days	double	time from breast cancer diagnosis to first radiotherapy session	no negative values allowed	it might be calculated as the difference between the date of the breast cancer diagnosis and the first radiotherapy session (procedure) (see definitions in next sheets)	field calculated at individual level
procedure	**time_dx_to_chemotherapy_nm**	[time til first prescription/administration of a chemotherapy treatment]	required	none	days	double	time from breast cancer diagnosis to first prescription/administration of a chemotherapy treatment	no negative values allowed	it might be calculated as the difference between the date of the breast cancer diagnosis and the prescription/administration of chemotherapy treatment (see definitions in next sheets)	field calculated at individual level
procedure	**time_dx_to_inmunotherapy_nm**	[time til first prescription/administration of a immunotherapy (a.k.a biological) treatment]	required	none	days	double	time from breast cancer diagnosis to first prescription/administration of a inmunotherapy treatment	no negative values allowed	calculated as the difference between the date of the breas cancer diagnosis and the prescription/administration of inmunotherapy treatment (see definitions in next sheets)	field calculated at individual level
drug exposure	**time_dx_to_hormonotherapy_nm**	[time til first prescription/administration of a hormonotherapy treatment]	required	none	days	double	time from breast cancer diagnosis to first prescription/administration of a hormonotherapy treatment	no negative values allowed	calculated as the difference between the date of the breas cancer diagnosis and the prescription/administration of hormonotherapy treatment (see definitions in next sheets)	field calculated at individual level
observation period	**period**	[time period]	required	none	month	integer	natural month	yyyy-mm	calculated as the natural month in which each patient recieved any of the aforementioned types of treatment	field calculated at aggregated level

Synthetic dataset

PHIRI Federated Analysis Application (Docker)

- Common Data Model
- **Synthetic Dataset**
- Quality Analysis (scripts)
- Analysis (scripts)
- Outputs recollection & synthesis

patient_id	ttm_type_cd	age_nm	time_dx_to_surgery_nm	time_dx_to_radiotherapy_nm	time_dx_to_chemotherapy_nm	time_dx_to_hormonotherapy_nm	time_dx_to_immunotherapy_nm	period	socecon_lvl_cd	country_cd	country_origin_cd	hospital_id
1	1	59	21	NA	NA	NA	4	1	0	ESP	ESP	20
2	2	60	13	15	NA	NA	6	21	0	ESP	ESP	27
3	2	54	53	2	NA	NA	104	20	0	ESP	ESP	68
4	5	51	6	3	3	NA	18	8	0	ESP	ESP	98
5	3	72	NA	NA	1	NA	33	11	0	ESP	ESP	67
6	2	59	1	0	NA	NA	13	17	0	ESP	ESP	89
7	4	52	1	NA	NA	10	21	17	0	ESP	ESP	90
8	2	67	0	17	NA	NA	0	10	0	ESP	ESP	45
9	5	51	28	41	0	NA	2	33	1	ESP	ESP	5
10	2	57	1	53	NA	NA	0	11	0	ESP	ESP	88
11	5	58	53	16	7	NA	96	19	0	ESP	ESP	68
12	4	49	4	NA	NA	10	15	22	0	ESP	ESP	57
13	4	36	20	NA	NA	6	3	12	0	ESP	ESP	16
14	1	52	19	NA	NA	NA	8	7	0	ESP	ESP	17
15	4	64	0	NA	NA	1	13	22	0	ESP	ESP	13
16	4	46	116	NA	NA	107	61	27	0	ESP	ESP	75
17	1	65	3	NA	NA	NA	7	5	0	ESP	ESP	80
18	5	50	5	2	4	NA	12	14	0	ESP	ESP	54
19	4	42	10	NA	NA	4	52	29	0	ESP	ESP	40
20	5	68	32	2	93	NA	0	2	0	ESP	ESP	33
21	2	51	0	14	NA	NA	0	31	0	ESP	ESP	39
22	3	54	NA	NA	14	NA	0	21	0	ESP	ESP	94
23	3	44	NA	NA	37	NA	4	22	1	ESP	ESP	12
24	4	61	76	NA	NA	222	33	31	0	ESP	ESP	16
25	4	71	0	NA	NA	0	6	9	1	ESP	ESP	51
26	2	70	2	0	NA	NA	15	20	0	ESP	ESP	3
27	1	67	38	NA	NA	NA	35	32	0	ESP	ESP	90
28	5	56	81	319	9	NA	81	20	0	ESP	ESP	69
29	4	58	4	NA	NA	5	37	6	0	ESP	ESP	50
30	1	52	91	NA	NA	NA	178	1	0	ESP	ESP	41
31	5	57	0	1	0	NA	1	10	0	ESP	ESP	38
32	3	57	NA	NA	0	NA	2	21	0	ESP	ESP	92
33	1	47	92	NA	NA	NA	0	10	0	ESP	ESP	89
34	2	75	12	30	NA	NA	7	12	0	ESP	ESP	42
35	3	55	NA	NA	9	NA	2	20	0	ESP	ESP	75
36	5	43	38	72	22	NA	6	18	0	ESP	ESP	67
37	2	44	76	59	NA	NA	0	29	0	ESP	ESP	66
38	2	55	11	15	NA	NA	0	20	0	ESP	ESP	87

breast_cancer_ttm_delays_synthe

Listo

Data quality assessment

PHIRI Federated Analysis Application (Docker)

- Common Data Model
- Synthetic dataset
- **Quality Analysis (scripts)**
- Analysis (scripts)
- Outputs recollection & synthesis

Using Python's **Pandas Profiling API**

PHIRI delayed_ttm_breast_cancer

Overview

Overview | Warnings 13 | Reproduction

Dataset statistics

Number of variables	13
Number of observations	19356
Missing cells	42583
Missing cells (%)	16.9%
Total size in memory	3.8 MiB
Average record size in memory	208.0 B

Overview | Warnings 13 | Reproduction

Warnings

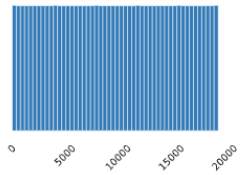
country_cd	has constant value "ESP" — Constant
country_origin_cd	has constant value "ESP" — Constant
time_dx_to_surgery_nm	has 3909 (20.2%) missing values — Missing
time_dx_to_radiotherapy_nm	has 11585 (59.9%) missing values — Missing
time_dx_to_chemotherapy_nm	has 11558 (59.7%) missing values — Missing
time_dx_to_hormonotherapy_nm	has 15531 (80.2%) missing values — Missing
patient_id	has unique values — Unique
time_dx_to_surgery_nm	has 1960 (10.1%) zeros — Zeros
time_dx_to_radiotherapy_nm	has 1003 (5.2%) zeros — Zeros
time_dx_to_chemotherapy_nm	has 1653 (8.5%) zeros — Zeros
time_dx_to_hormonotherapy_nm	has 656 (3.4%) zeros — Zeros
time_dx_to_immunotherapy_nm	has 3083 (15.9%) zeros — Zeros
socecon_lvl_cd	has 17421 (90.0%) zeros — Zeros

Variables

patient_id
Real number ($\mathbb{R}_{\geq 0}$)

UNIQUE

Distinct	19356	Minimum	1
Distinct (%)	100.0%	Maximum	19356
Missing	0	Zeros	0
Missing (%)	0.0%	Zeros (%)	0.0%
Infinite	0	Negative	0
Infinite (%)	0.0%	Negative (%)	0.0%



Analytical workflows

PHIRI Federated Analysis Application (Docker)

- Common Data Model
- Synthetic dataset
- Quality Analysis (scripts)
- **Analysis (scripts)**
- Outputs recollection & synthesis

Run Chunk | Run Above

```r
```{r load_libraries}
## 3. Load required libraries ####
library(DBI)
library(dplyr)
library(htmlTable)
library(magrittr)
library(utils)
library(tidyverse)
library(kableExtra)
library(wrapr)
library(plyr)


```
```

Run Chunk | Run Above

```r
```{r load_data}
con <- dbConnect(RSQLite::SQLite(), "/home/phiri/analysis-scripts/inputs/database/database.db")
df <- dbReadTable(con, "perinatal_health")

```
```

Run Chunk | Run Above

```r
```{r indicators}

indicator_names <- c()
n_per_year22<-df %>% filter(GA >= 22, VITAL != 4, VITAL!= 1, VITAL !=99) %>% group_by(year) %>% tally()
total_per_year22 <- df  %>% filter(GA >= 22) %>% group_by(year) %>% tally()
n_per_year22$indicator <- "aa_22weeks"

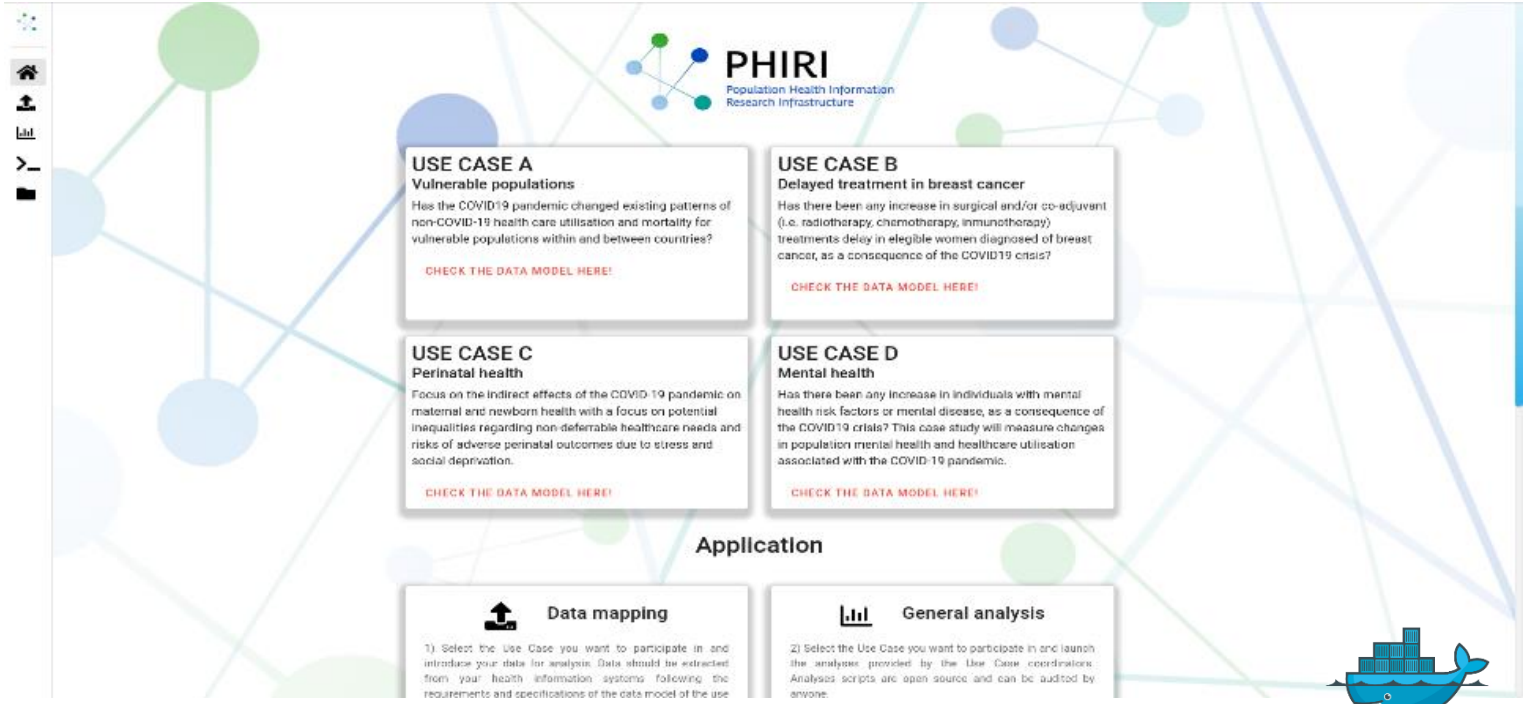
n_per_year24<-df %>% filter(GA >= 24, VITAL != 4, VITAL!= 1, VITAL !=99) %>% group_by(year) %>% tally()
total_per_year24 <- df  %>% filter(GA >= 24) %>% group_by(year) %>% tally()
n_per_year24$indicator <- "ab_24weeks"

n_per_year28<-df %>% filter(GA >= 28, VITAL != 4, VITAL!= 1, VITAL !=99) %>% group_by(year) %>% tally()
total_per_year28 <- df  %>% filter(GA >= 28) %>% group_by(year) %>% tally()
n_per_year28$indicator <- "ac_28weeks"
```
```

Containerised solution ready for deployment

PHIRI Federated Analysis Application (Docker)

- Common Data Model
- Synthetic dataset
- Quality Analysis (scripts)
- Analysis (scripts)
- **Use Case Deployment**



Running local analyses and results devolution

PHIRI Federated Analysis Application (Docker)

- Common Data Model
- Synthetic dataset
- Quality Analysis (scripts)
- Analysis (scripts)
- **Outputs recollection & synthesis**

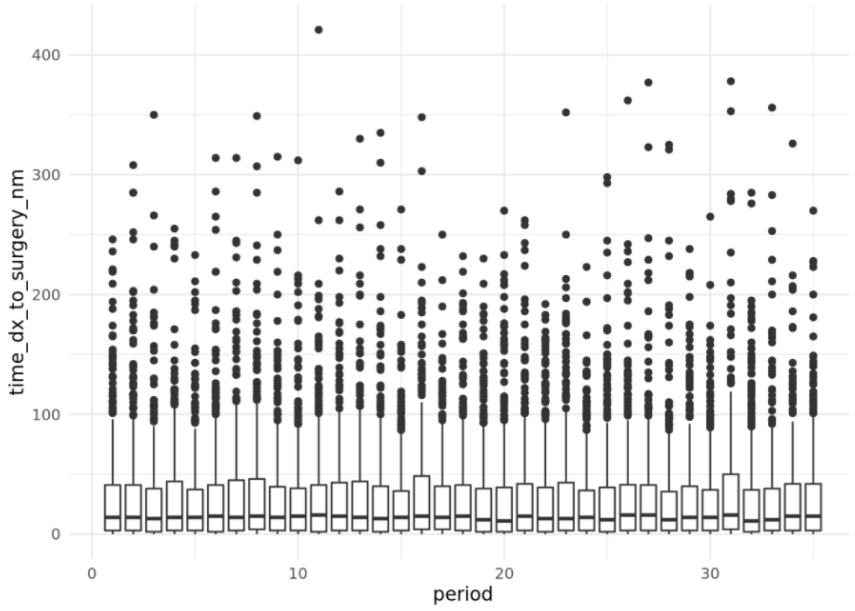
Use Case B report example with synthetic data

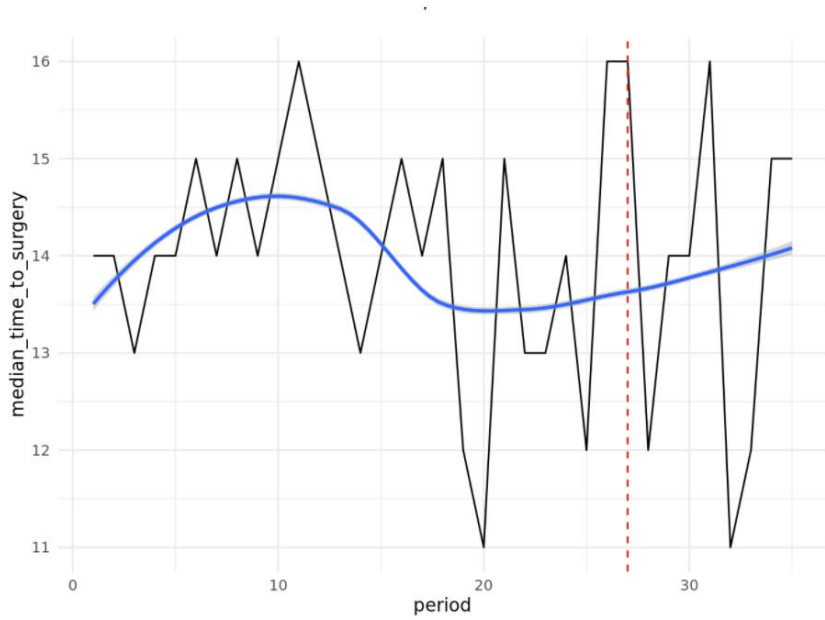
Estupiñán-Romero, Francisco; González-Galindo, Javier; Bernal-Delgado, Enrique

16/6/2021

Exploratory Analysis (Local)

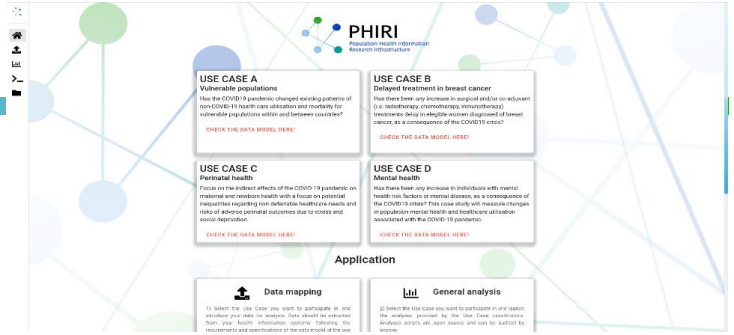
Distribution of times from diagnosis of breast cancer to treatment



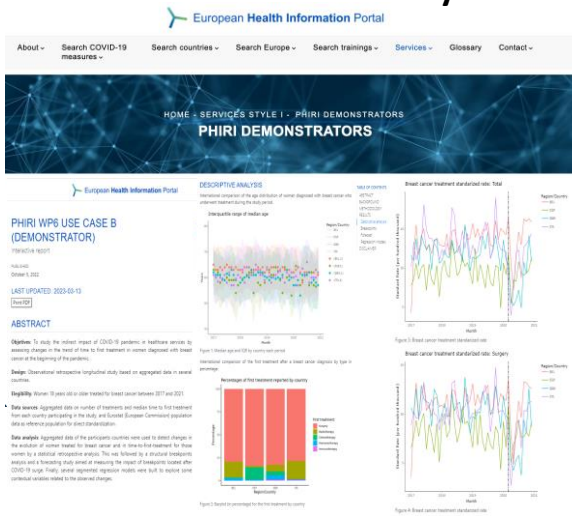


Achievements

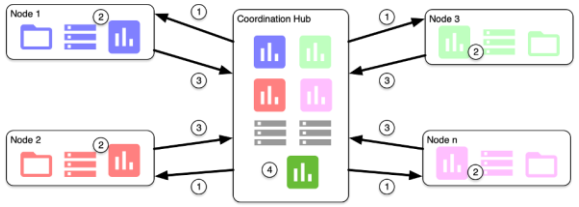
App for deployment



Do it yourself



Federated architecture



LOST pipeline for PICO-t

Others are using PHIRI

PHIRI

Population Health Information Research Infrastructure

Thank you for your attention

Enrique Bernal-Delgado, IACS, ES
Martin Thissen, RKI, DE

ROBERT KOCH INSTITUT

IACS Instituto Aragonés de Ciencias de la Salud

www.phiri.eu

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PHIRI Federated Analysis Application (Docker) User Interface Tutorial

ROBERT KOCH INSTITUT

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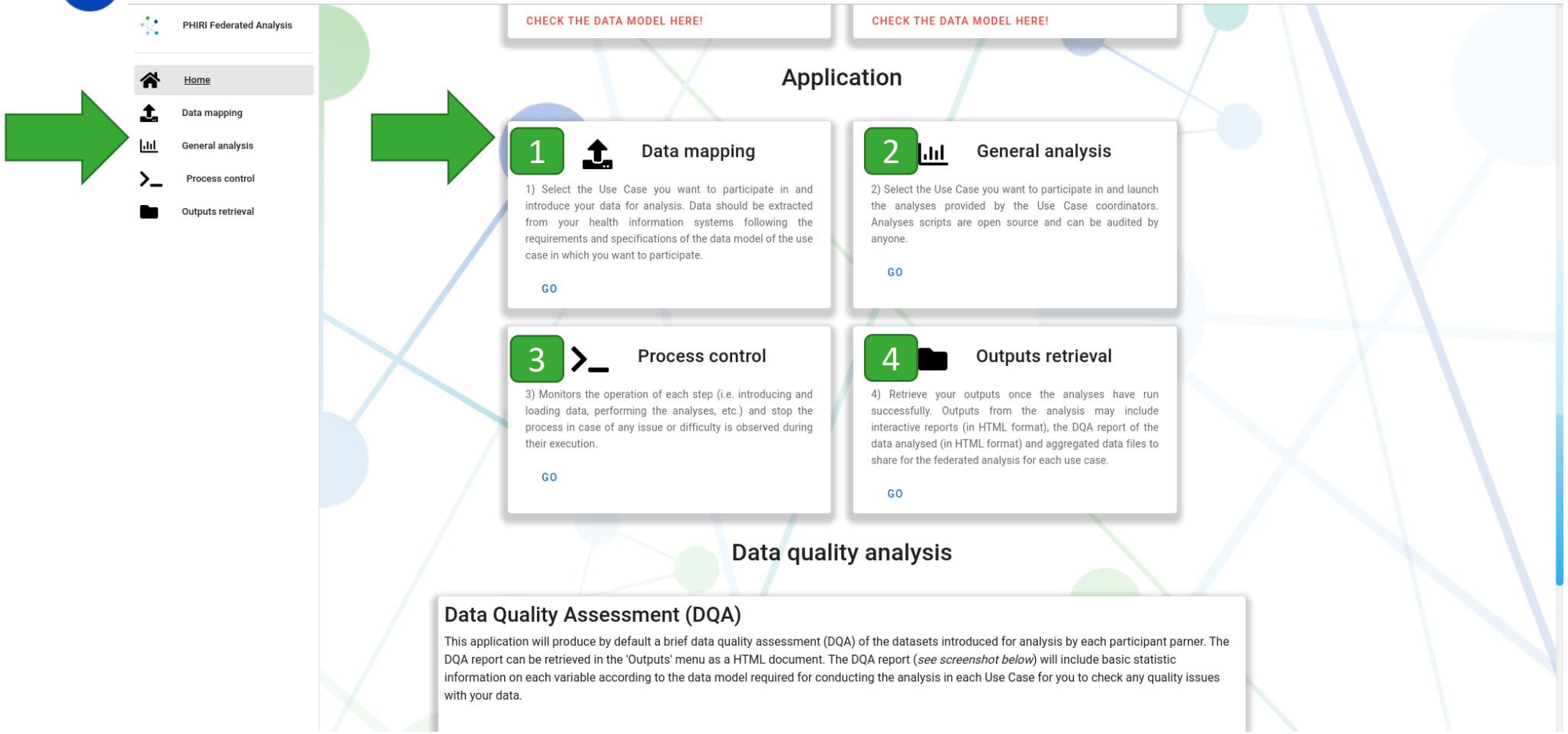
PHIRI Federated Analysis Application (Docker) User Interface



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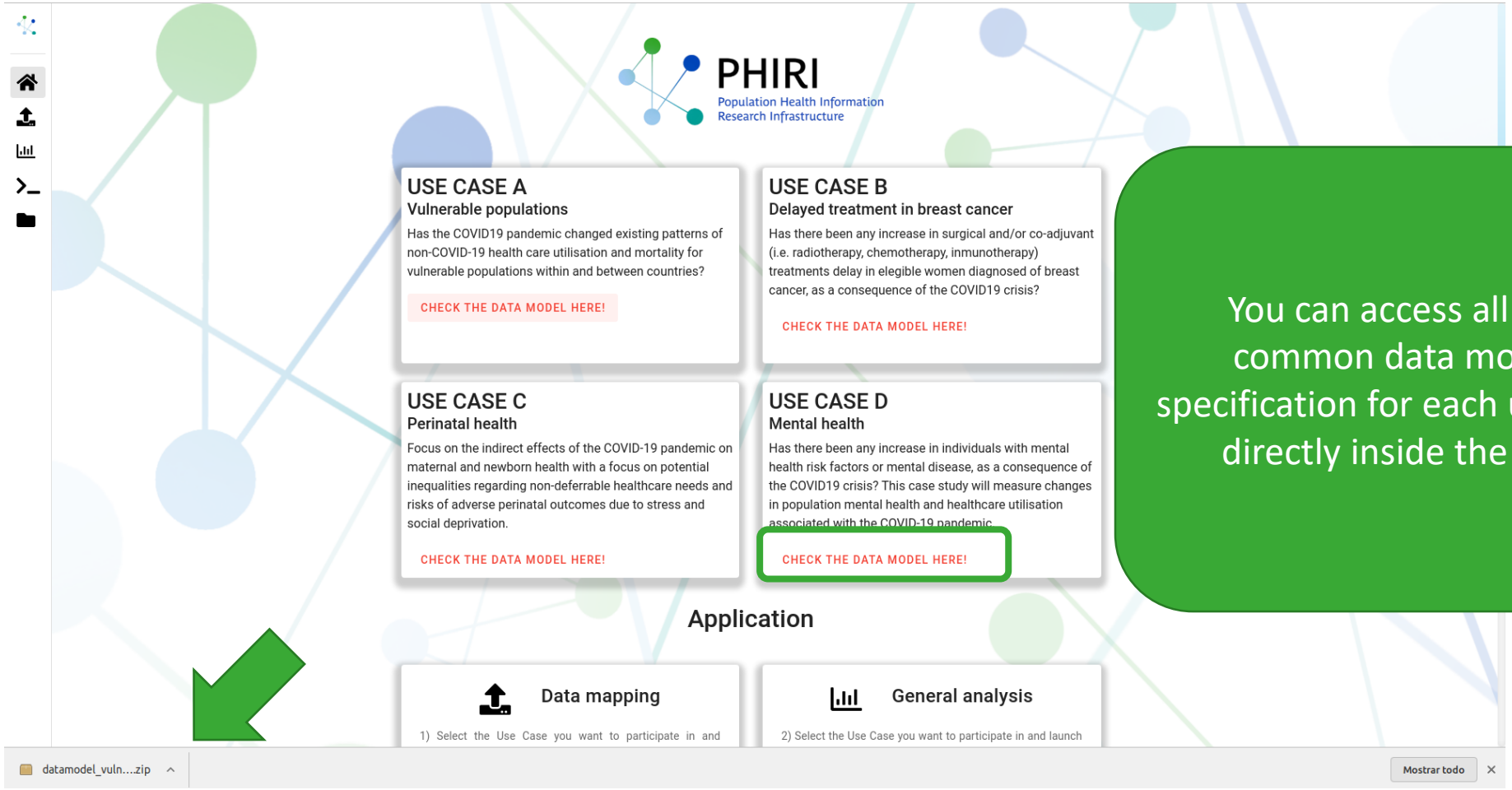
PHIRI Federated Analysis Application (Docker) User Interface



You can access all the common data model specification for each use case directly inside the app

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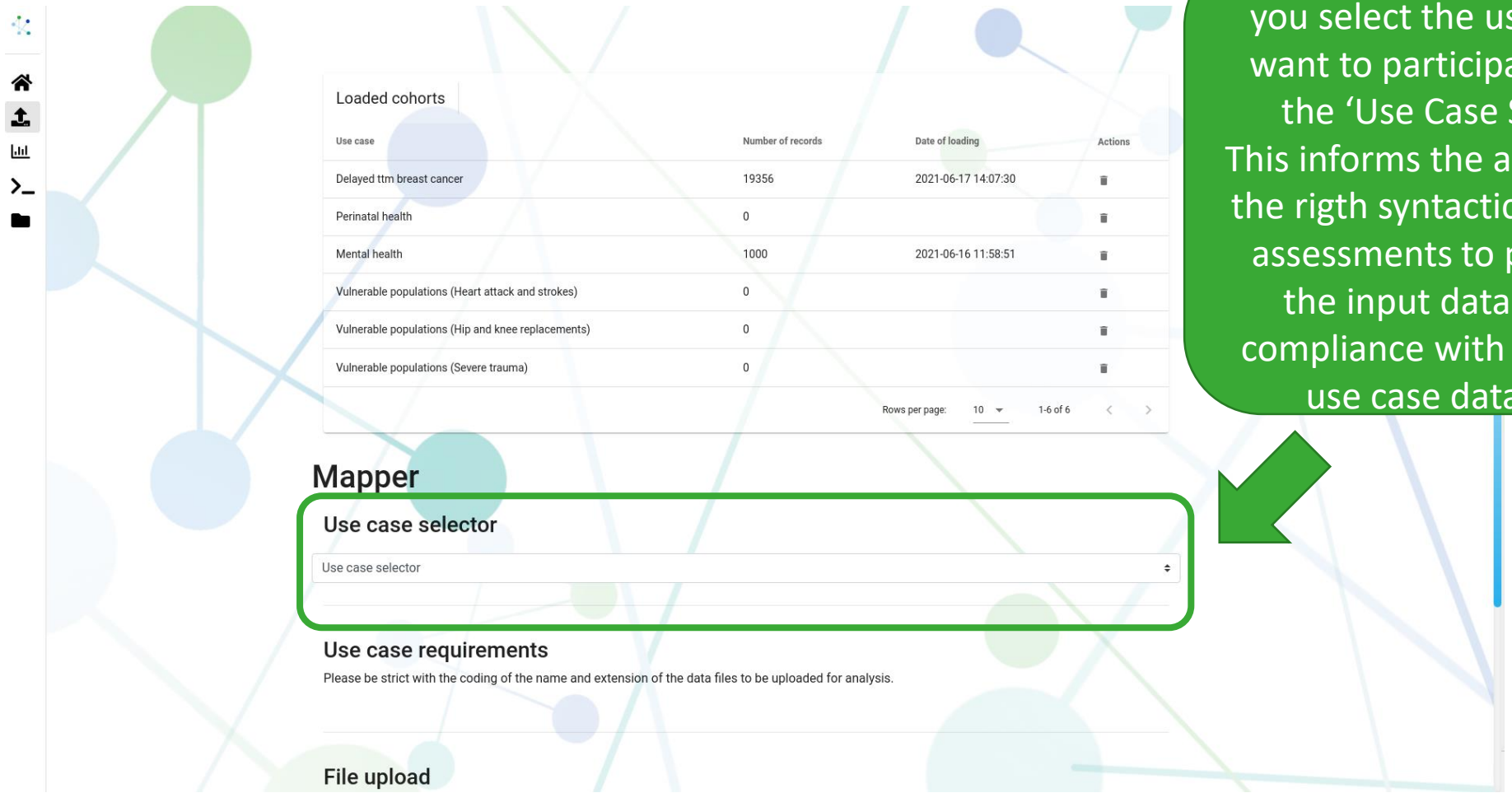
PHIRI Federated Analysis Application (Docker) User Interface



To participate in a use case, you select the use case you want to participate in using the 'Use Case Selector'. This informs the application of the rigth syntactic and quality assessments to perform on the input data to check compliance with the specific use case data model

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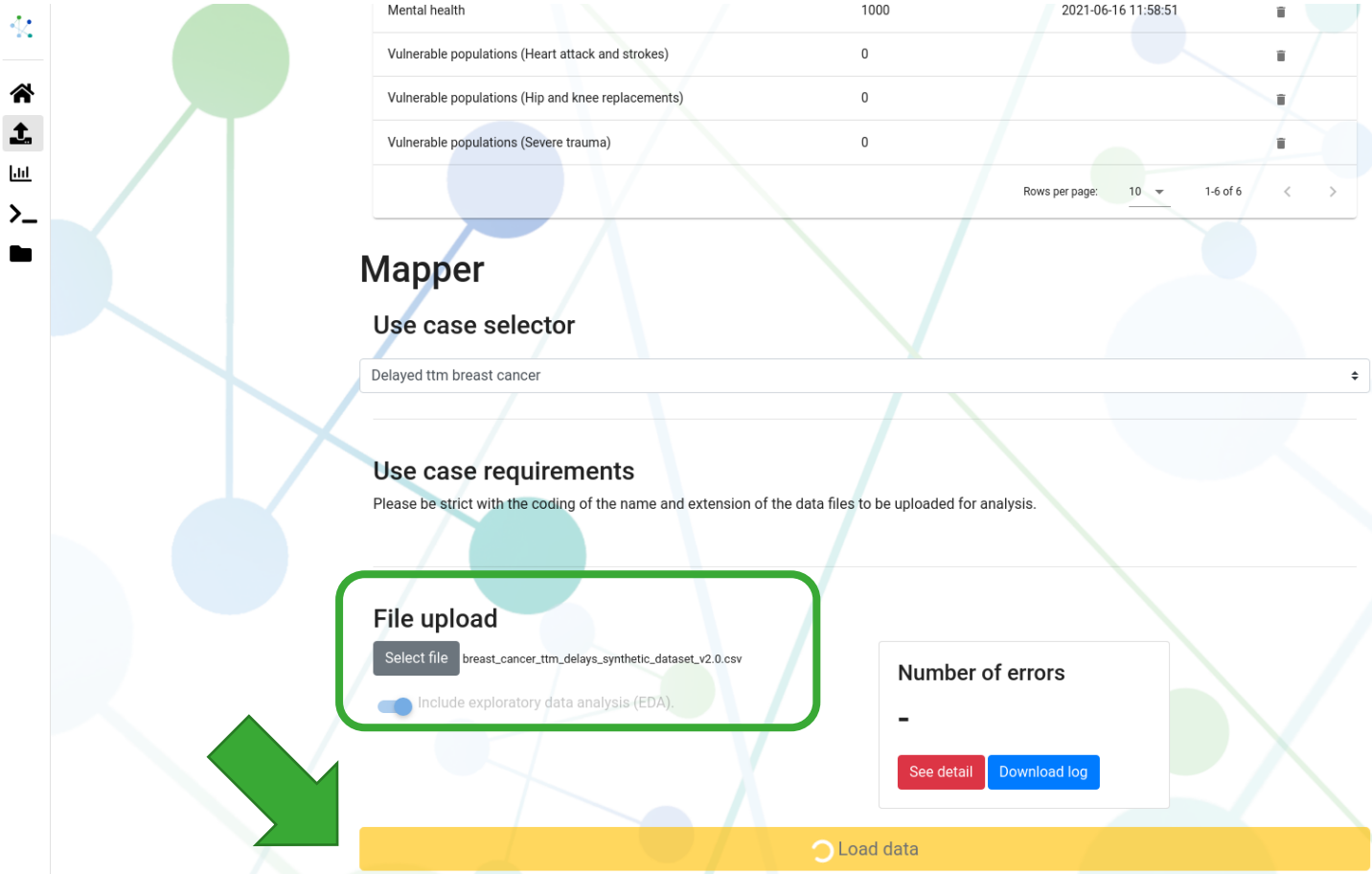
PHIRI Federated Analysis Application (Docker) User Interface



Once you select the use case, you can load your input data selecting the file from your system and clicking on the 'Load data' button

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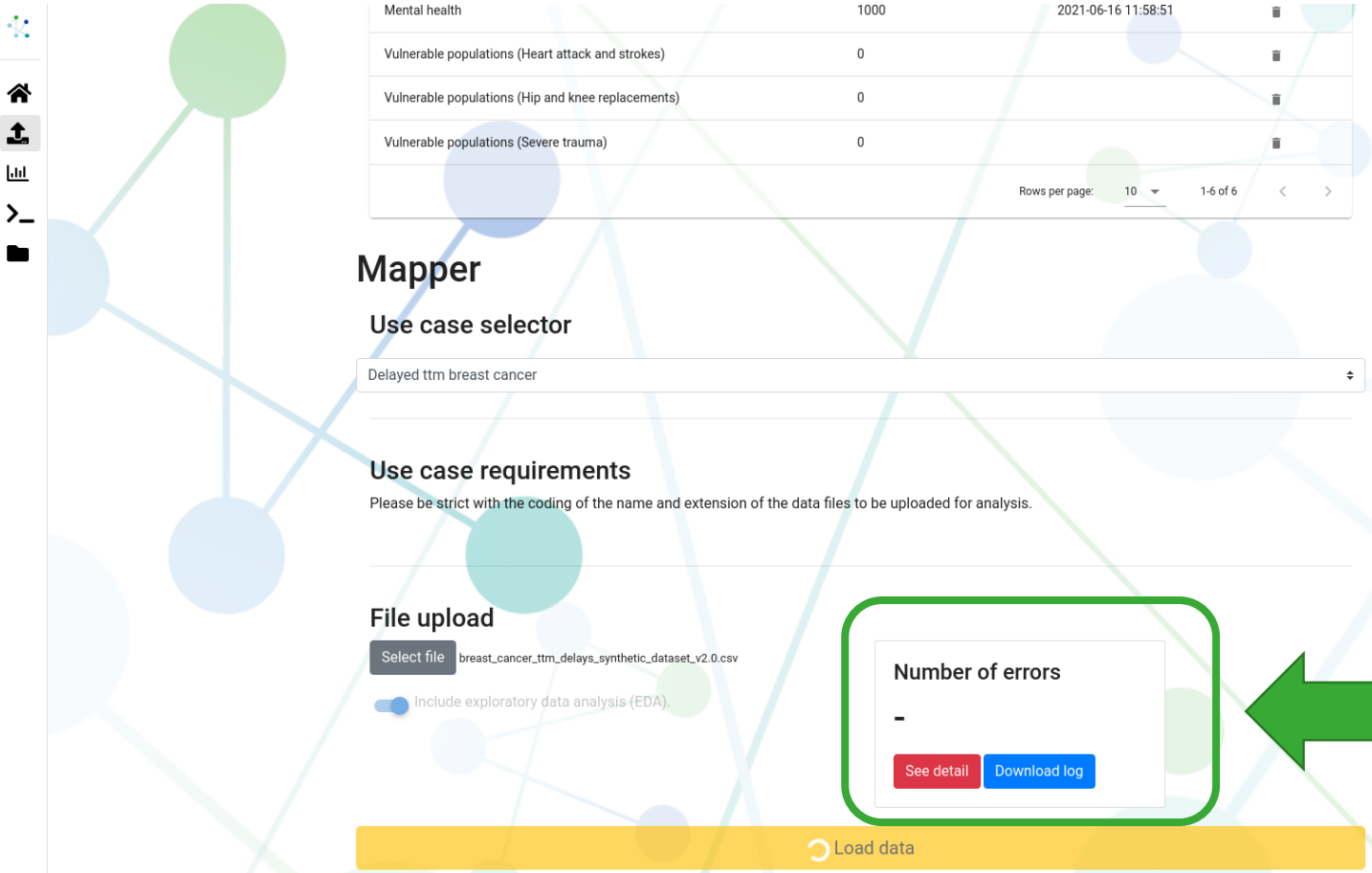
PHIRI Federated Analysis Application (Docker) User Interface



The PHIRI app checks whether your input data syntacticaly complies with the specifications of the data model for the use case you selected before and if it does not comply, it produces an error log file with information on the registers (lines) and variables (columns) that are not compliant for you to check and correct

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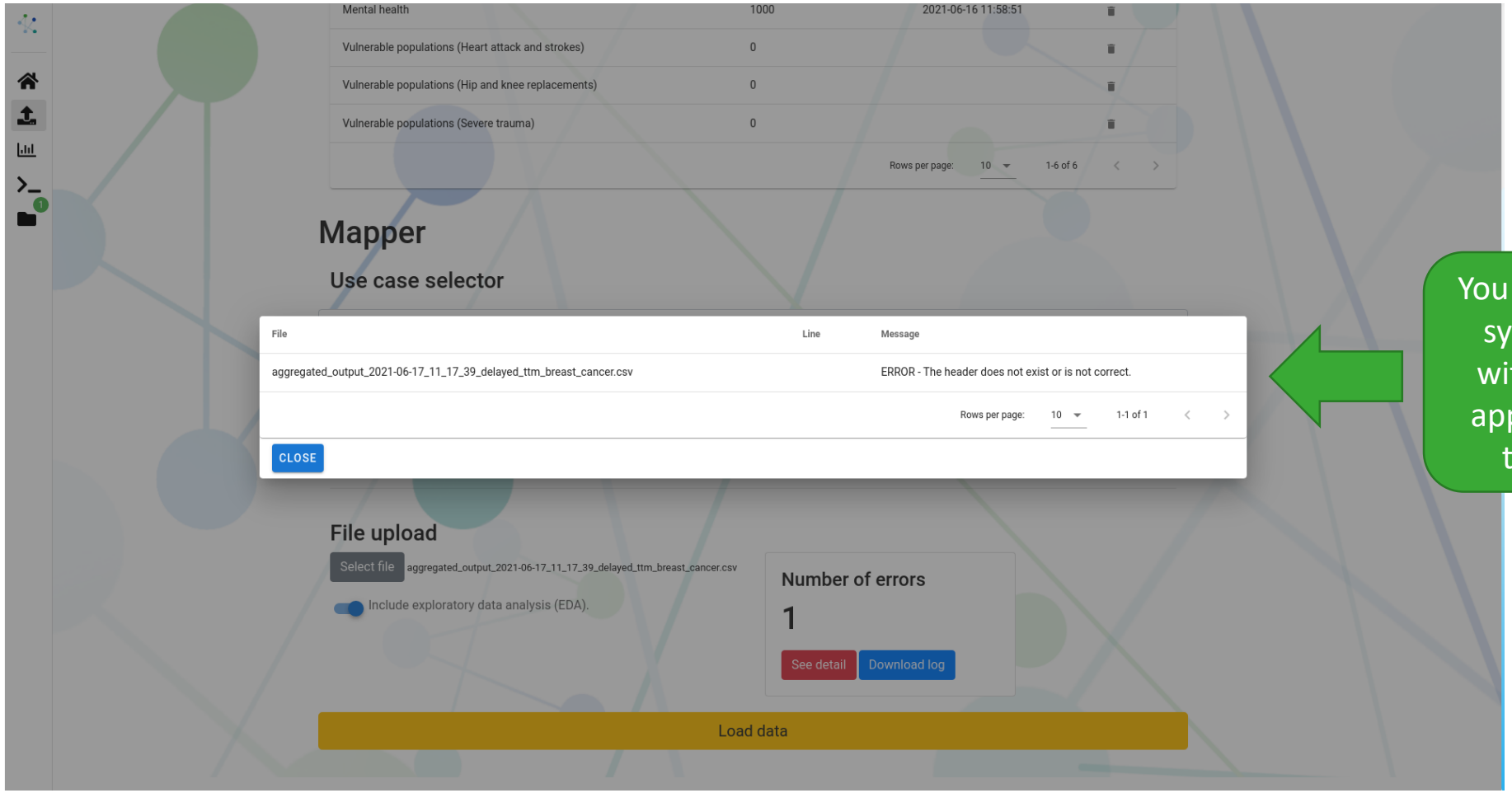
PHIRI Federated Analysis Application (Docker) User Interface



You can review the syntactic errors within the PHIRI app or download the error log

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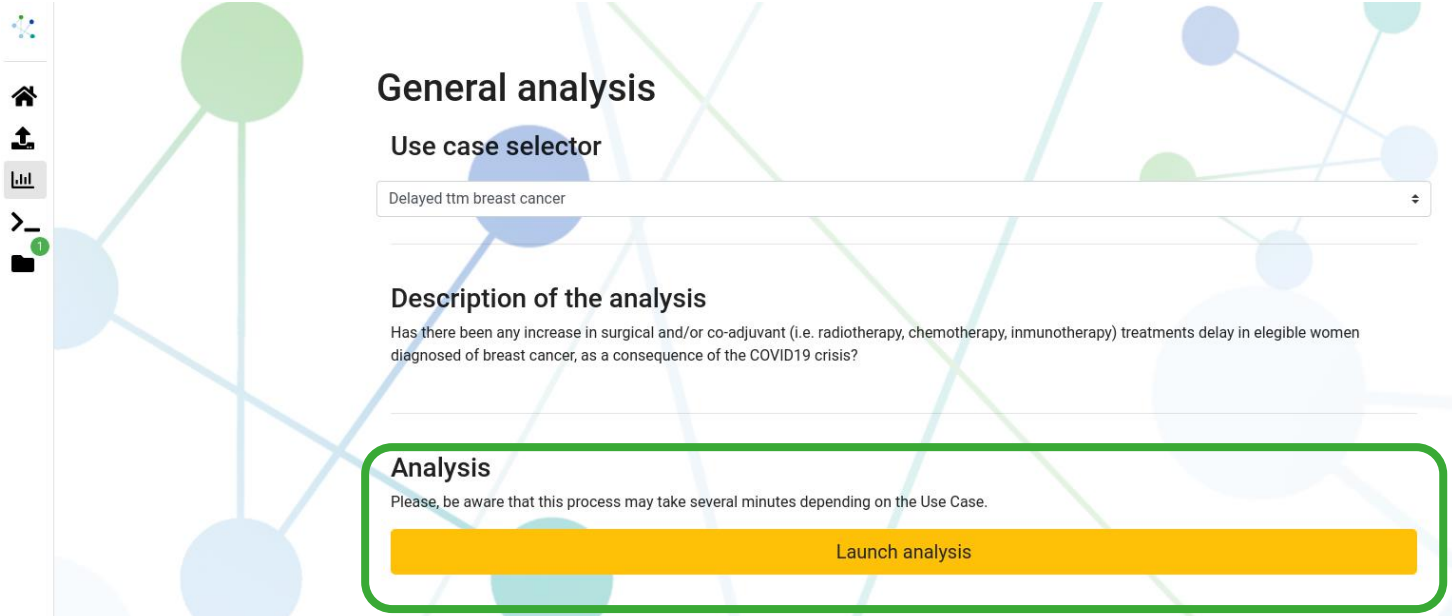
PHIRI Federated Analysis Application (Docker) User Interface



Next step if there are no syntactic errors will be to 'Launch' the analysis.
The PHIRI app automatically launches the Data Quality Analysis in the background upon mapping the data without errors but you have to explicitly launch the analysis.

As you can be participating in multiple use cases, the PHIRI app enables you to map several data inputs (one per use case) and select for which use case you want to launch the analysis.
Use the 'Use case selector' in the 'General Analysis' tab to select the use case you want to run and click on the 'Launch analysis' button

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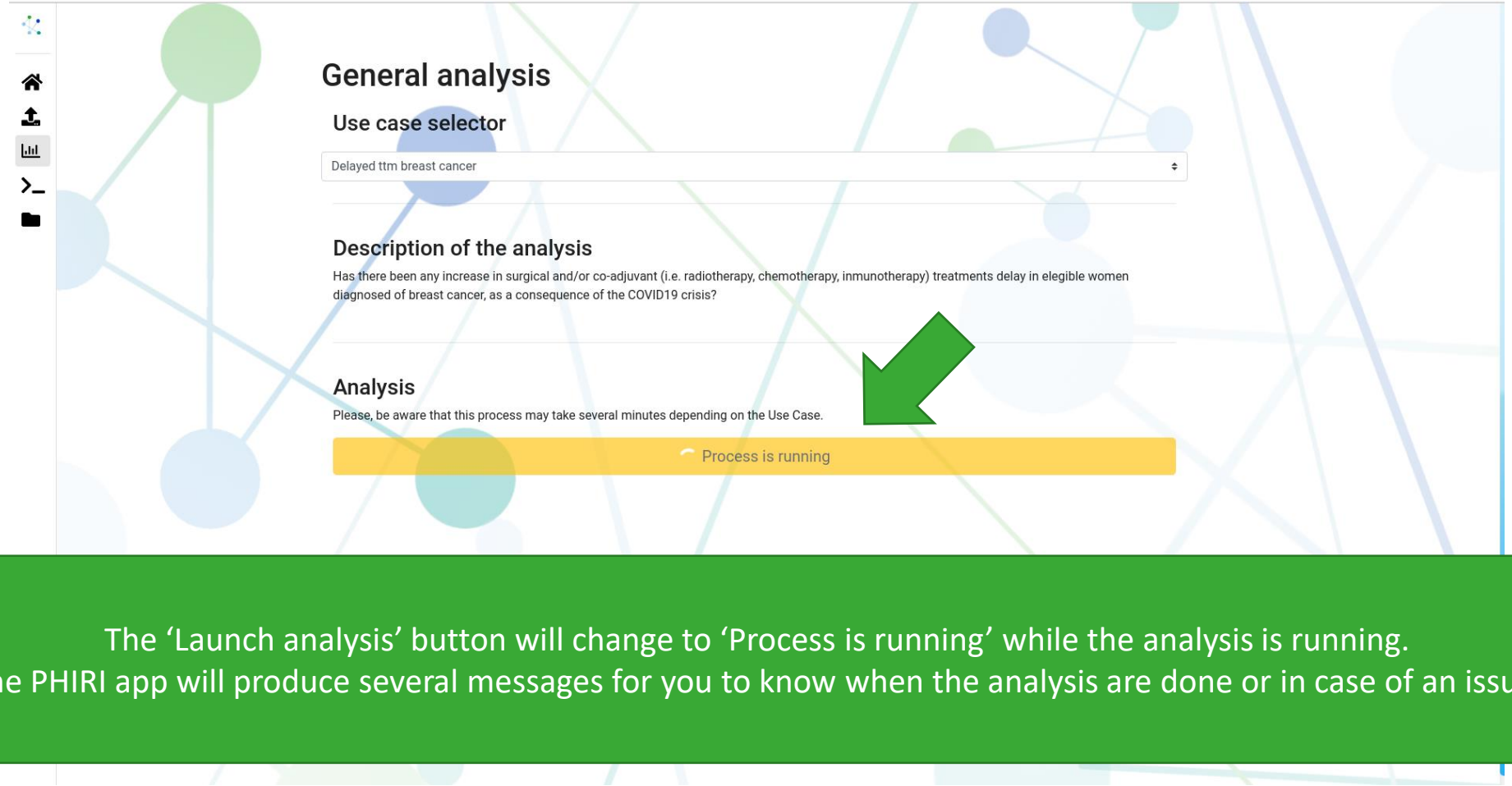
PHIRI Federated Analysis Application (Docker) User Interface



The ‘Launch analysis’ button will change to ‘Process is running’ while the analysis is running.
The PHIRI app will produce several messages for you to know when the analysis are done or in case of an issue.

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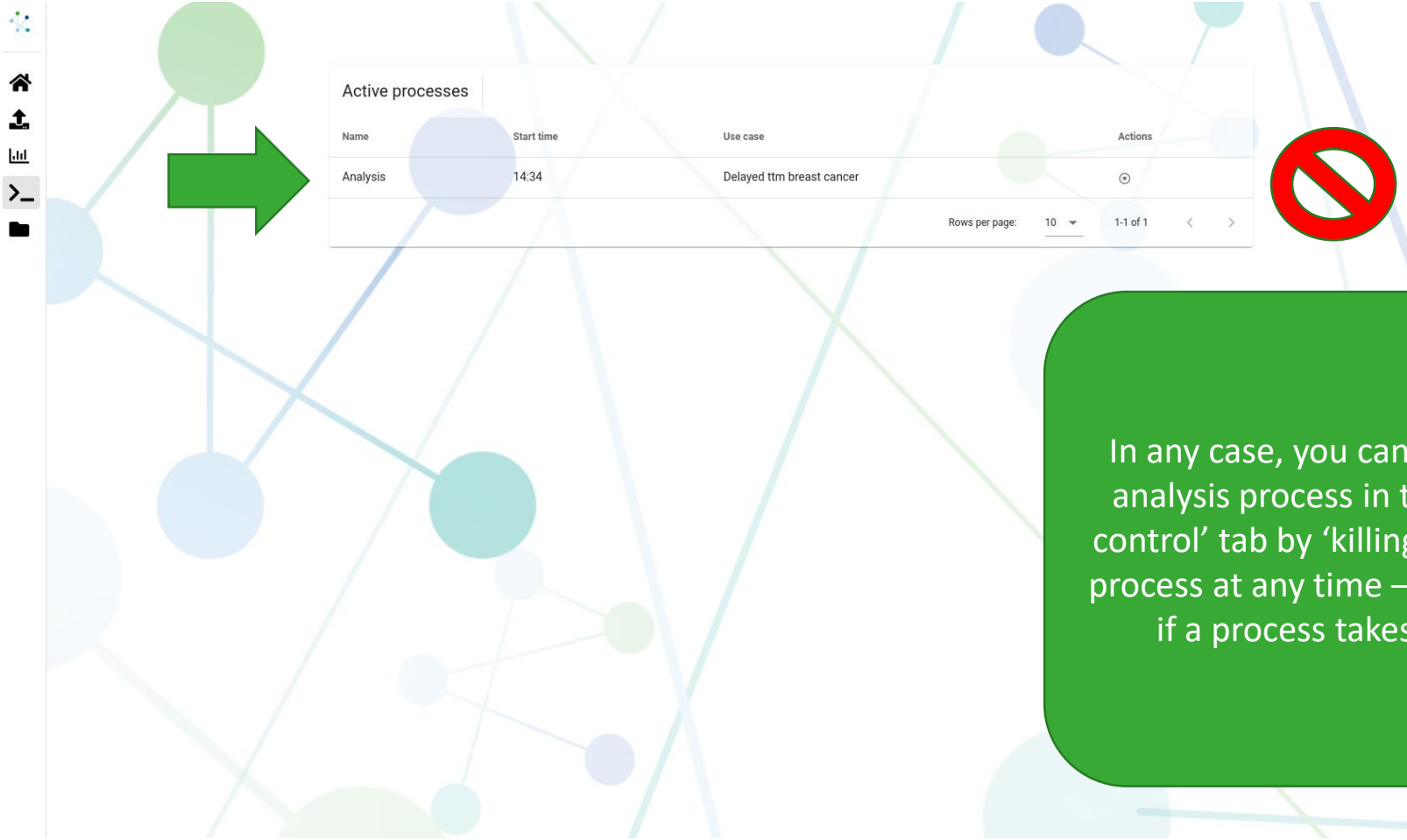
PHIRI Federated Analysis Application (Docker) User Interface



In any case, you can control the analysis process in the 'Process control' tab by 'killing/stopping' a process at any time – for instance, if a process takes to long.

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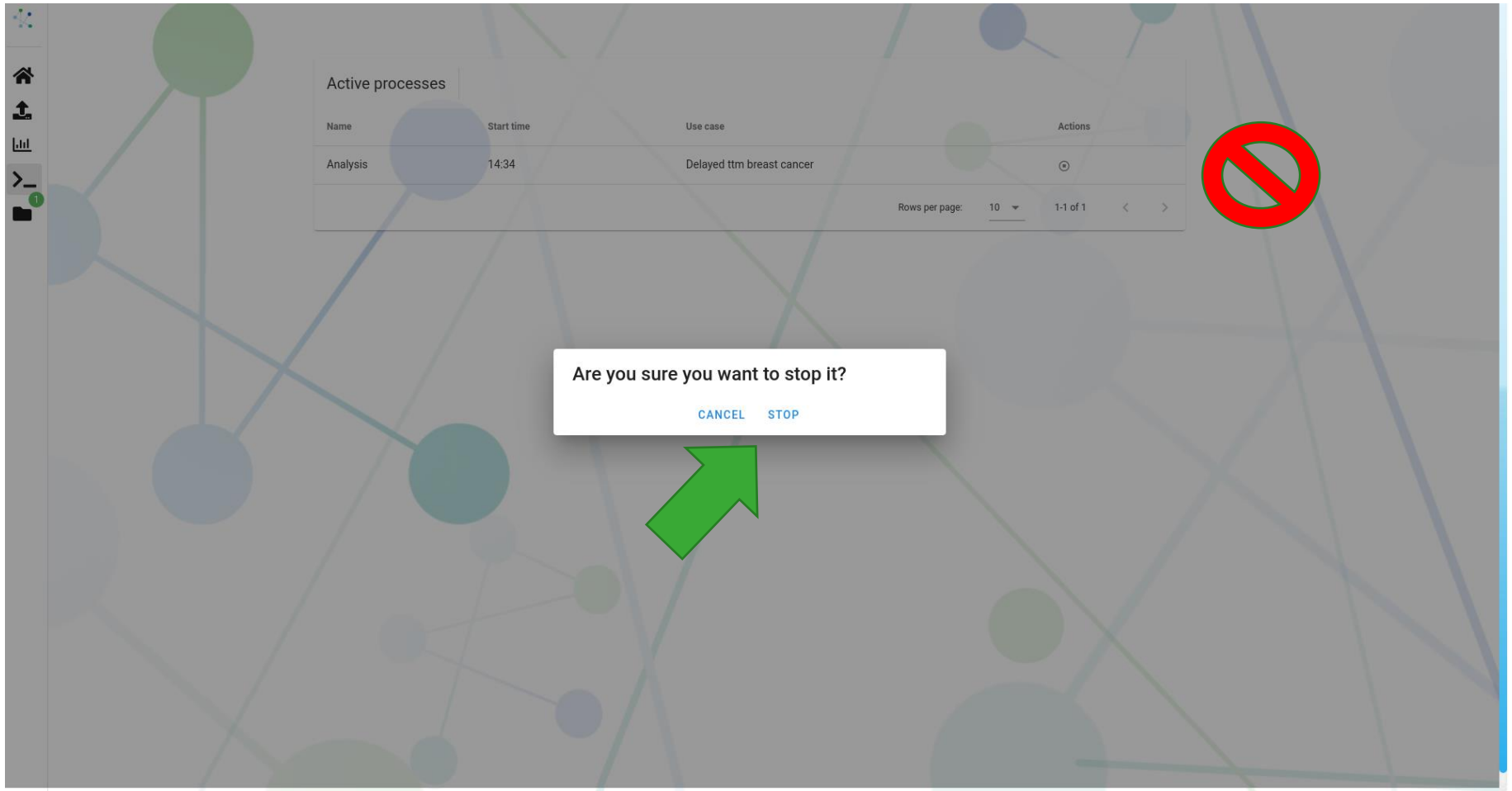
PHIRI Federated Analysis Application (Docker) User Interface



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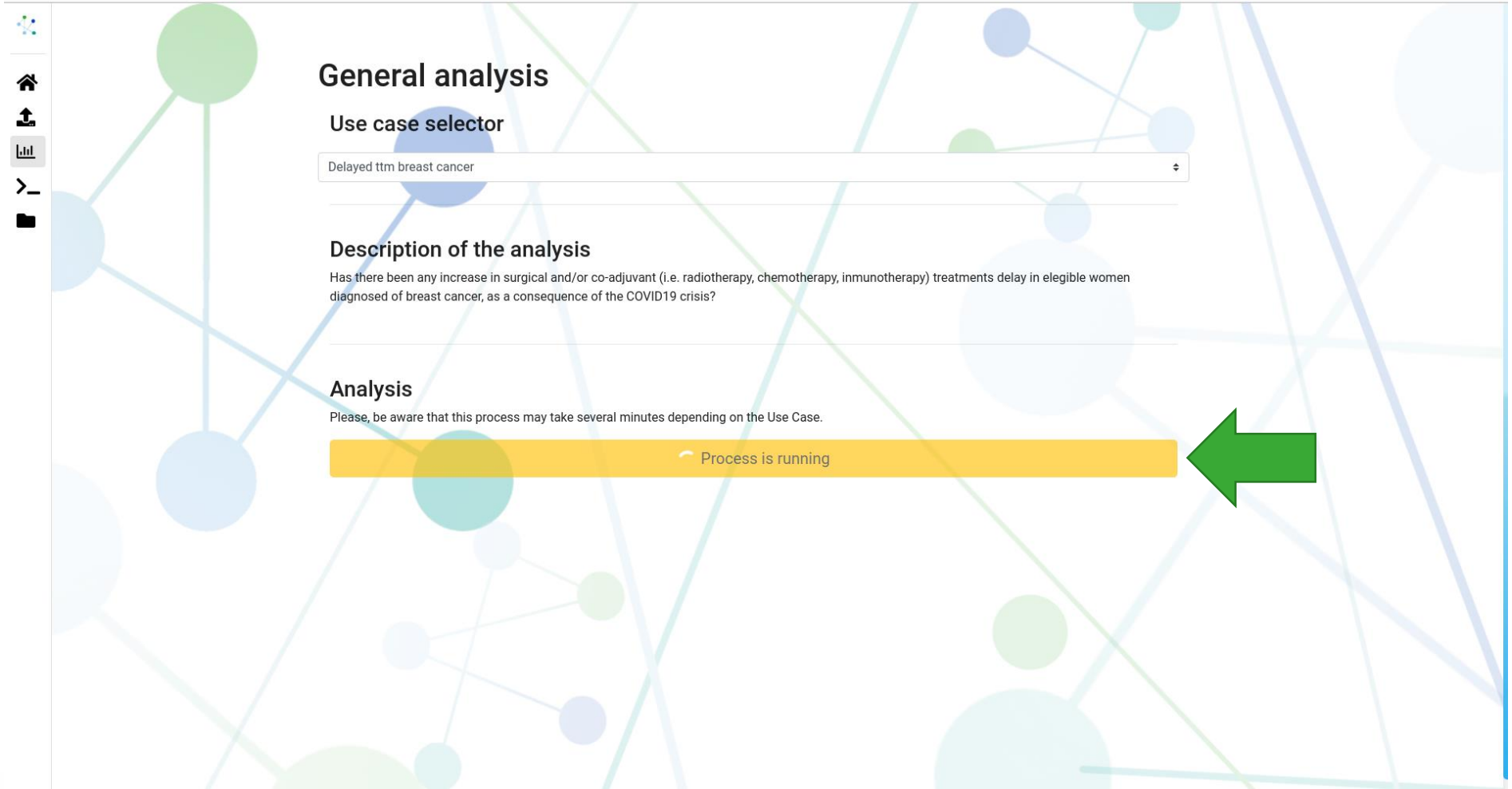

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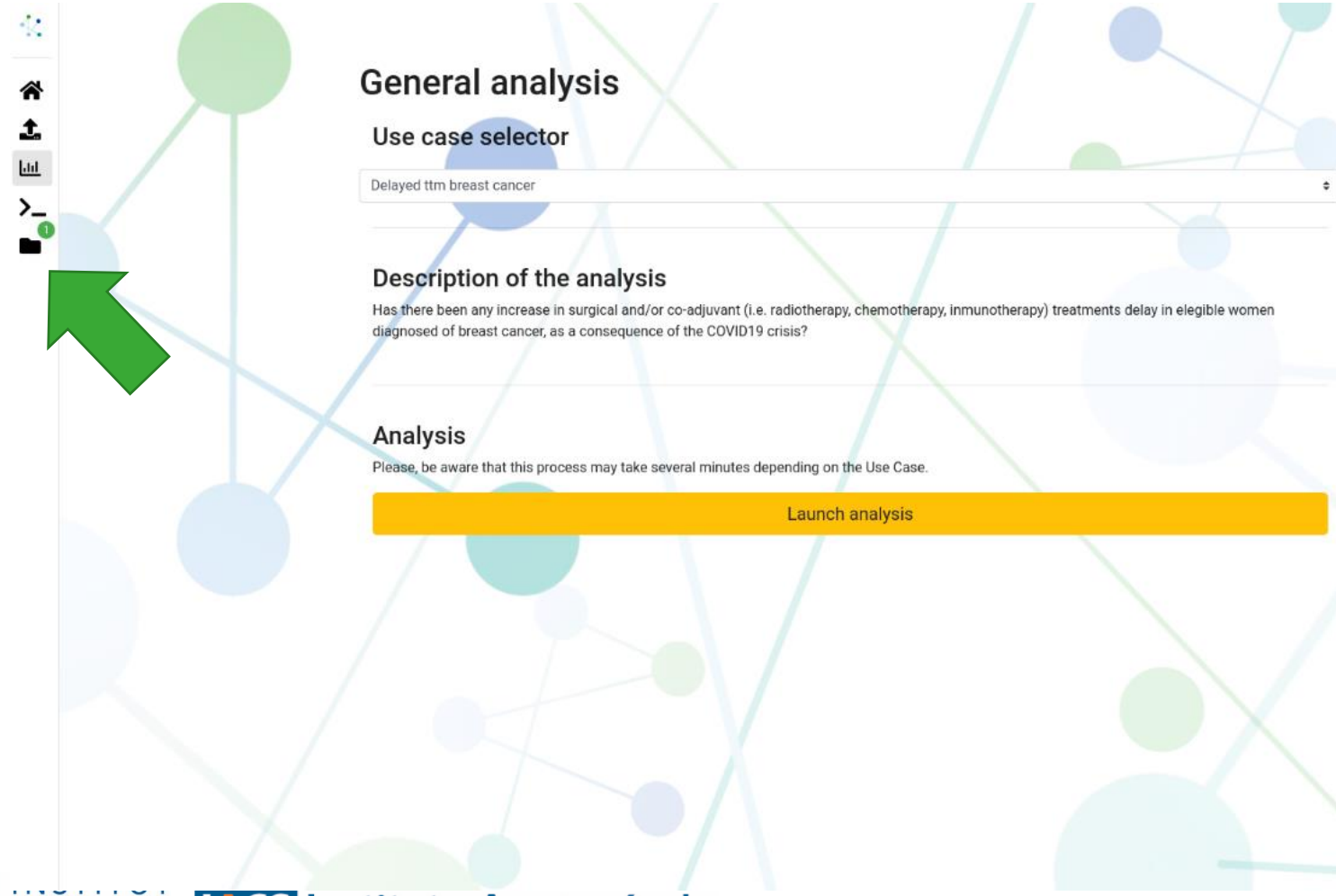

Once the analysis are done you can go to the 'Outputs retrieval' tab to check and download your outputs

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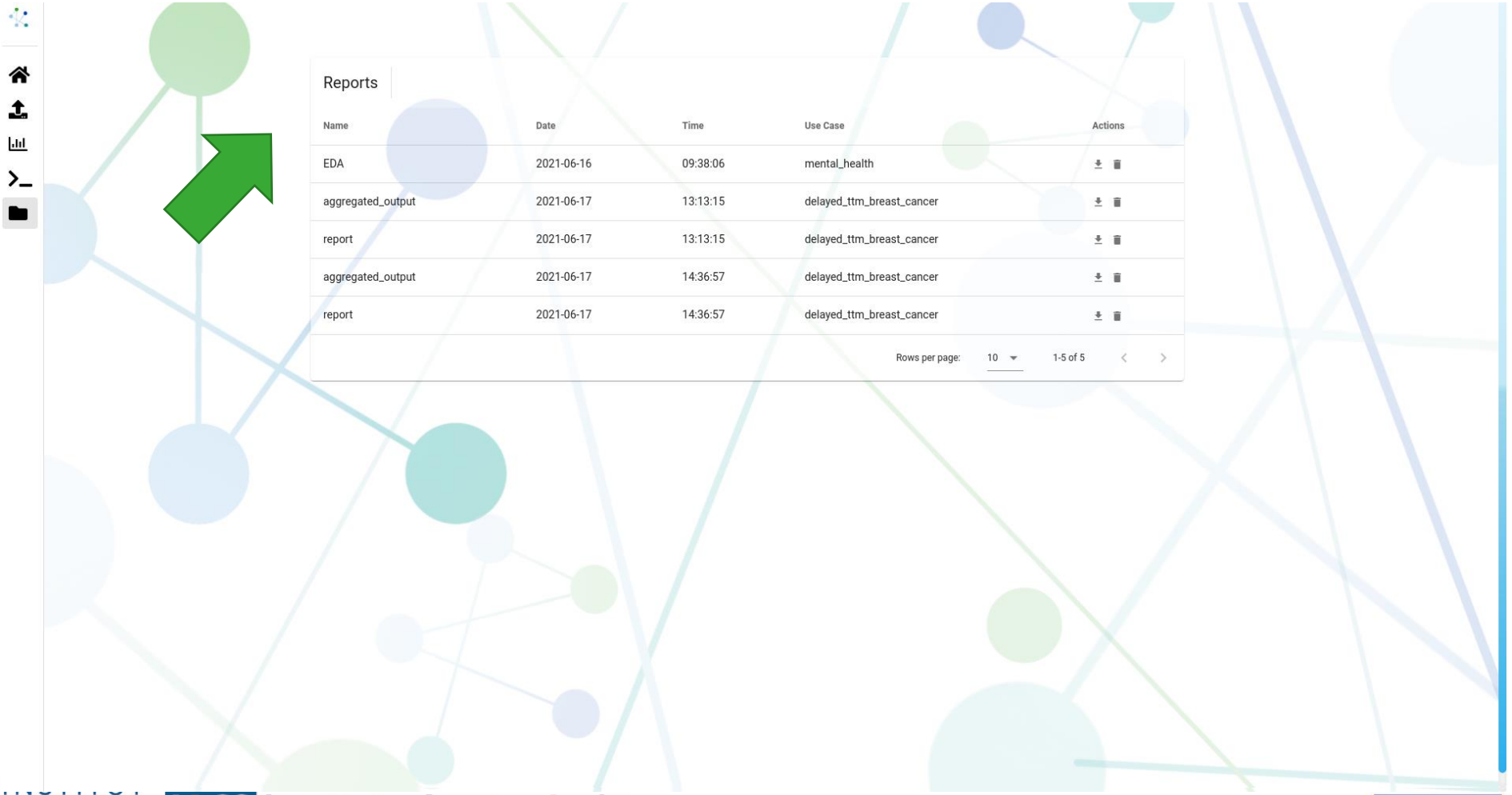
PHIRI Federated Analysis Application (Docker) User Interface



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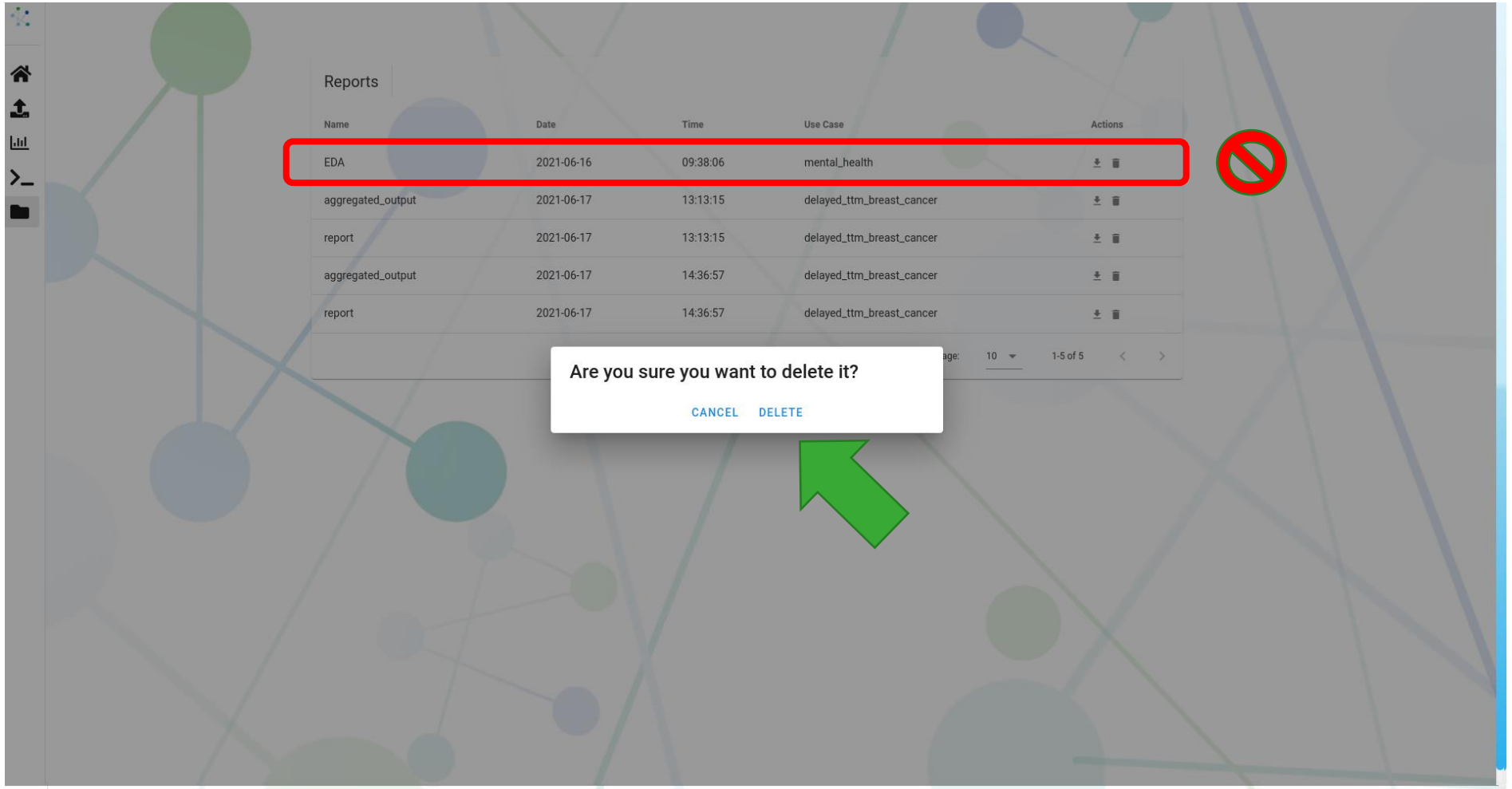

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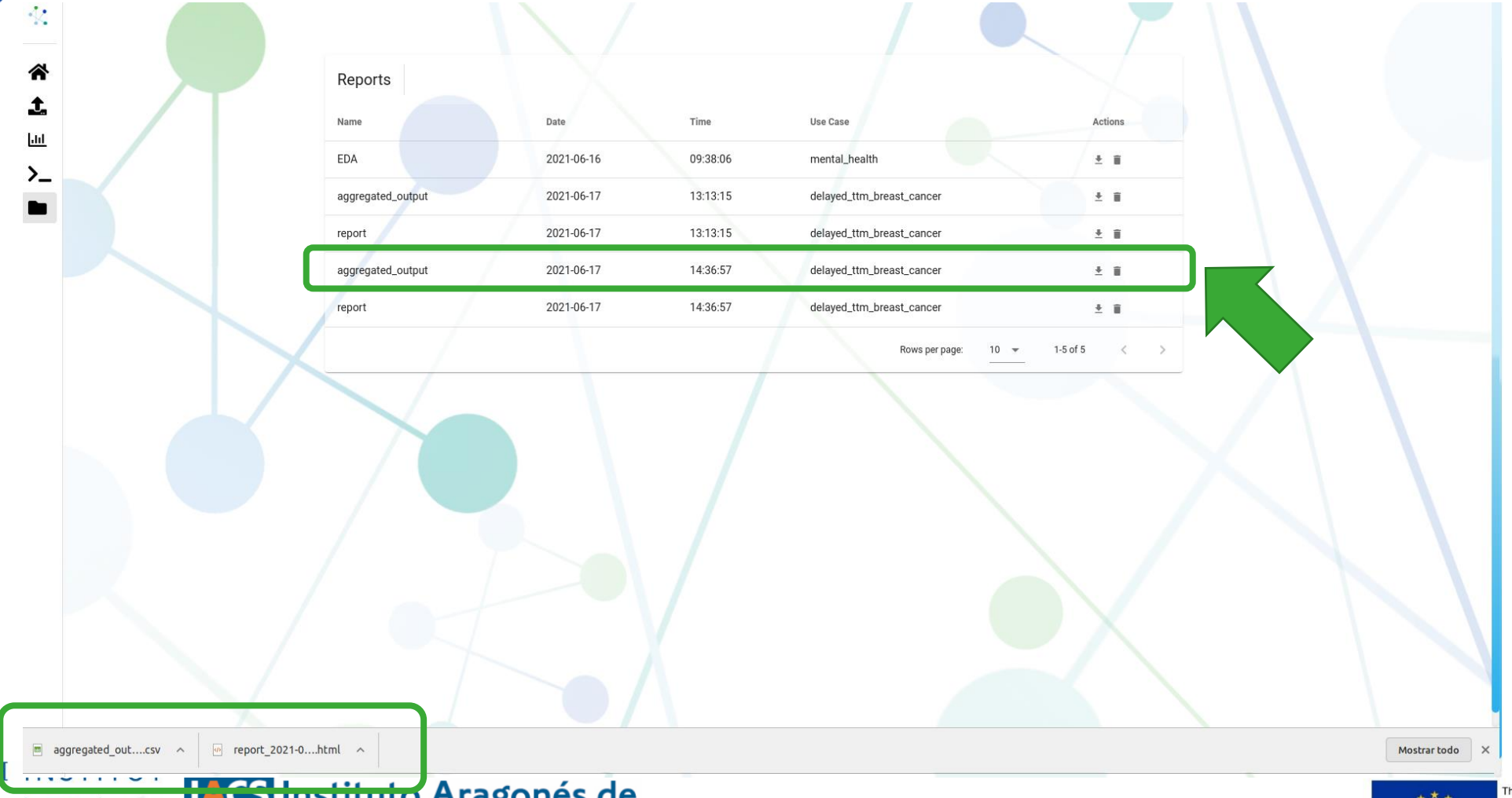
PHIRI Federated Analysis Application (Docker) User Interface



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PHIRI Federated Analysis Application (Docker)

- PHIRI app demo available at phiri.iacs.es

- Help-Desk
  - Technical/Implementation support:
    - To: festupinnan.iacs@aragon.es

THANKS!

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Replicating a use case in a federated research infrastructure

https://github.com/cienciadedatosysalud/tutorial_cdmb_EUPHA

https://github.com/cienciadedatosysalud/by-covid_baseline-use-case_EUPHA

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