HIVCAre Documentation

Epidemiology and Inpatient Care Characteristics of HIV-positive Cancer Patients in German university hospitals

Bastian Reiter

2023-07-12

Table of contents

Part I

About this Documentation

FAIR Principles

(Sandve et al. 2013)

FAIR Principles

STROBE Statement

STROBE Statement

Part II

Project Information

1 Project Synopsis

1.1 Project Background

- Infection with Human Immunodeficiency Virus (HIV) and its consequential acquired immune deficiency syndrome (AIDS) entail an increased risk of developing cancer. The associated malignancies are commonly classified into AIDS-defining cancer (AD, e.g. Kaposi sarcoma) and HIV-associated non-AIDS-defining cancer (NAD, e.g. Hodgkin lymphoma).
- Establishment of effective antiretroviral therapy (ART) is considered a major driver of the steep decline in AD cancer incidence since the 1990s, however the risk of NAD cancer in persons living with HIV (PLWH) remains elevated compared to non-infected individuals. Today cancer is the leading cause of death among the infected population, a fact that has in part been attributed to the considerable rise in life expectancy.
- Medical care of HIV-positive cancer patients involves management of complex interactions between ART and potential side effects, anti-infective therapy as well as cancer treatment in a latently immunocompromised host.
- Currently no specific care structures have been established in German hospitals to meet this medical challenge.
- Exploration of Real World Data could provide insights into epidemiology and inpatient care characteristics of HIV-positive cancer patients.
- We analyze data curated in the context of a federal law (Krankenhausentgeltgesetz, KHEntG), that requires all German hospitals to transmit the so-called §21-data-set to a semi-public institute (InEK GmbH) under management of central health system organization.
- The correspondent data base is curated and hosted by hospital infrastructure and can be accessed by Data Integration Centers.
- Using federated analysis techniques ensures a high level of data privacy and maintains data sovereignty of the participating sites.

1.2 Research Objectives

Main Objective: Explore epidemiology and inpatient care characteristics of HIV-positive cancer patients

- Describe cancer occurrence in HIV-positive patients over time stratified by cancer category
- Explore possible differences in care characteristics between HIV-negative and HIV-positive cancer patients
- Explore differences in course of therapy between HIV-negative and HIV-positive cancer patients

2 Project Governance

2.1 Full Project Title

Epidemiology and Inpatient Care Characteristics of HIV-positive Cancer Patients in German university hospitals (HIVCAre)

2.2 Project Initiation

Prof. Dr. Jörg Janne Vehreschild
Melanie Stecher, PhD
Stefanie Andreas, M.Sc.
Dr. Daniel Maier

2.3 Project Supervision

Prof. Dr. Jörg Janne Vehreschild
Department of Medicine
Hematology and Medical Oncology
University Hospital Frankfurt
Goethe University Frankfurt

2.4 Project Administration

Bastian Reiter
Department of Medicine
Hematology and Medical Oncology
University Hospital Frankfurt
Goethe University Frankfurt

2.5 Research Associates

Last Name	First Name	Primary Affiliation
Albashiti	Fady	MeDIC LMU, Zentrum für Medizinische Datenintegration und -analyse, Universit
Andreas	Stefanie	Department of Medicine, Hematology and Medical Oncology, University Hospital
Aubele	Fabio	MeDIC LMU, Zentrum für Medizinische Datenintegration und -analyse, Universit
Hagedorn	Marlien	MeDIC LMU, Zentrum für Medizinische Datenintegration und -analyse, Universit
Laukhuf	Andrea	Data Integration Center, University Hospital Freiburg, Freiburg
Maier	Daniel	Department of Medicine, Hematology and Medical Oncology, University Hospital
Müller	Matthias	Department of Internal Medicine 2, Infectious Diseases, University Hospital Freib
Reiter	Bastian	Department of Medicine, Hematology and Medical Oncology, University Hospital
Roider	Julia	Division of Infectious Diseases, University Hospital Munich (LMU), Munich
Sauer	Gabriel	Department of Internal Medicine I, University Hospital of Cologne, Cologne
Schulze	Nick	German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Colog
Seybold	Ulrich	Division of Infectious Diseases, University Hospital Munich (LMU), Munich
Stecher	Melanie	Norwegian Institute of Public Health, Oslo
Stephan	Christoph	HIVCENTER, Medical HIV Treatment and Research Unit, Johann Wolfgang Goe
Vehreschild	Jörg Janne	Department of Medicine, Hematology and Medical Oncology, University Hospital
Wehrle	Julius	Data Integration Center, University Hospital Freiburg, Freiburg

2.6 Participating Institutions

City	Hospital	University	Institution
Cologne	Uniklinik Köln	Universität zu Köln	Medical Data Inte
Frankfurt/Main	Universitätsklinikum Frankfurt	Goethe-Universität Frankfurt	Datenintegrationsz
Freiburg	Universitätsklinikum Freiburg	Albert-Ludwigs-Universität Freiburg	Datenintegrationsz
Munich	LMU Klinikum	Ludwig-Maximilians-Universität	Zentrum für Mediz

2.7 Funding

There is no third-party funding for this project.

2.8 Conflicts of Interest

We have no conflicts of interest to disclose.

2.9 Publication

The study results will be published in cooperation with all associates.

3 Study Design

HIVCAre is a multicenter retrospective cohort study, conducted on Real World Health Data from German university hospitals.

3.1 Study Cohort

Data of patients admitted to the following university hospitals (in alphabetical order):

City	Hospital	University
Cologne	Uniklinik Köln	Universität zu Köln
Frankfurt/Main	Universitätsklinikum Frankfurt	Goethe-Universität Frankfurt
Freiburg	Universitätsklinikum Freiburg	Albert-Ludwigs-Universität Freiburg
Munich	LMU Klinikum	Ludwig-Maximilians-Universität

3.1.0.1 Inclusion criteria

- Admitted between 01-01-2005 and 12-31-2019
- Aged at least 18 years at date of admission
- At least one documented ICD-10 code representing malignancy or HIV infection

3.1.0.2 Exclusion criteria

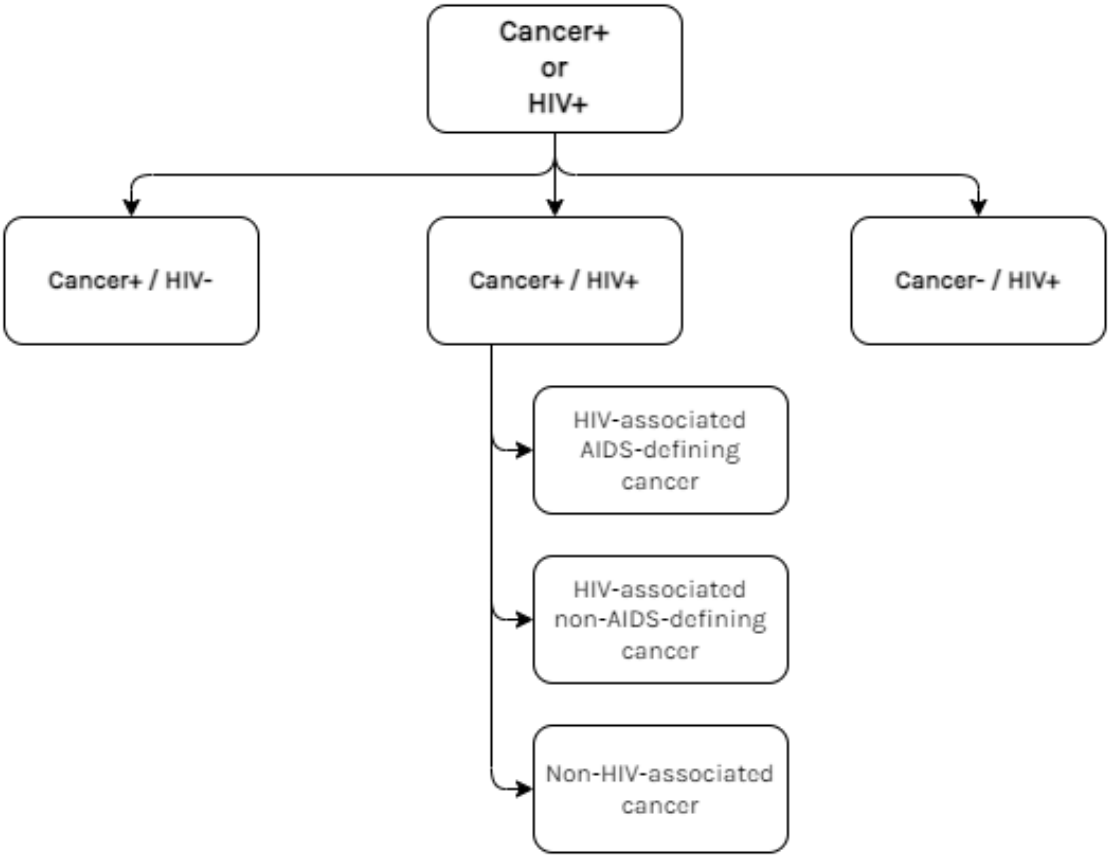
- Implausible documentation of ICD-10 codes

3.1.1 Stratification Model

3.2 Research Items

The following research items result from the research objectives stated here.

Item	Compared Strata	Research Item
Epidemiology		
1	All main subgroups	Sample size over time
2	All main subgroups	Age distribution over time
3	All main subgroups	Gender distribution over time
4	All main subgroups	Spatial distribution
7	Cancer+/HIV+	Occurrence of different HIV-associated cancer diagnoses over tim
8	Cancer+/HIV-	Occurrence of different HIV-associated cancer diagnoses over tim
9	Cancer+/HIV+	Projection of HIV-associated cancer diagnoses
10	Cancer+/HIV+	Occurrence of AIDS in cancer patients, stratified by cancer categ
11	Cancer+/HIV+	Occurrence of AIDS code after chemotherapy
12	Cancer+/HIV+	Presumed order of diagnosis of HIV infection and cancer over tim
13	Cancer+/HIV- vs. Cancer+/HIV+	Age at presumed cancer onset
14	Cancer+/HIV- vs. Cancer+/HIV+	Cancer topography grouped by organ
15	Cancer+/HIV- vs. Cancer+/HIV+	Cancer topography grouped by organ over time
16	Cancer+/HIV- vs. Cancer+/HIV+	Projection of cancer topography grouped by organ
17	Cancer+/HIV- vs. Cancer+/HIV+	Cancer topography grouped by ICD-10 grouping
18	Cancer+/HIV- vs. Cancer+/HIV+	Cancer topography grouped by ICD-10 grouping over time
19	Cancer+/HIV- vs. Cancer+/HIV+	Projection of cancer topography grouped by ICD-10 grouping
20	Cancer+/HIV- vs. Cancer+/HIV+	Cancer occurrence grouped by entity
21	Cancer+/HIV- vs. Cancer+/HIV+	Cancer occurrence grouped by entity over time
22	Cancer+/HIV- vs. Cancer+/HIV+	Projection of cancer occurrence grouped by entity
25	Cancer+/HIV- vs. Cancer+/HIV+	Metastasis occurrence
31	Cancer+	Sequence in presumed HIV / Cancer / Metastasis / AIDS onset
Care Characteristics		
5	All main subgroups	Count of admissions per patient
6	All main subgroups	Mean length of stay per patient
Therapy		
23	Cancer+/HIV- vs. Cancer+/HIV+	Occurrence of cancer therapy modalities
24	Cancer+/HIV- vs. Cancer+/HIV+	Count of chemotherapy sessions
27	Cancer+/HIV- vs. Cancer+/HIV+	Occurrence of complications after chemotherapy
28	Cancer+/HIV- vs. Cancer+/HIV+	Time from chemotherapy to complication
32	Cancer+/HIV-	Sequence of cancer therapy modalities
33	Cancer+/HIV+	Sequence of cancer therapy modalities
Outcome		
26	Cancer+/HIV- vs. Cancer+/HIV+	Time from presumed cancer to presumed metastasis onset
29	Cancer+/HIV- vs. Cancer+/HIV+	Death after chemotherapy
30	Cancer+/HIV- vs. Cancer+/HIV+	Discharge reasons


Cancer+
or
HIV+
Cancer+ / HIV-
Cancer+ / HIV+
Cancer- / HIV+
HIV-associated
AIDS-defining
cancer
HIV-associated
non-AIDS-defining
cancer
Non-HIV-associated
cancer

4 Data Handling

4.1 Data Generation

Data accumulated in the context of a federal law called “Krankenhausentgeltgesetz”. This law requires all German hospitals to transmit the so-called §21-data-set to a semi-public institute (InEK GmbH) under management of central health system organizations.

4.2 Data Storage and Administration

Data Integration Centers (DIC) of university hospitals

4.2.1 Required Data Elements

	Primary data source	Data Type
Patient data		
Patient pseudonym	KHEntG-P21-data-set	character
Year of birth	KHEntG-P21-data-set	numeric
Sex	KHEntG-P21-data-set	character
Admission data		
Case pseudonym	KHEntG-P21-data-set	character
Date of admission	KHEntG-P21-data-set	date
Age at admission	KHEntG-P21-data-set	numeric
Date of discharge	KHEntG-P21-data-set	date
Reason of discharge	KHEntG-P21-data-set	character
Diagnostic data		
Diagnosis type	KHEntG-P21-data-set	character
ICD-10 version	KHEntG-P21-data-set	character
Primary ICD-10 code	KHEntG-P21-data-set	character
Secondary ICD-10 code	KHEntG-P21-data-set	character

Procedures data		
OPS Version	KHEntG-P21-data-set	character
OPS Code	KHEntG-P21-data-set	character
OPS Date	KHEntG-P21-data-set	date

4.3 Federated Analysis

4.4 Data Privacy and Security

4.5 Study Participant Consent

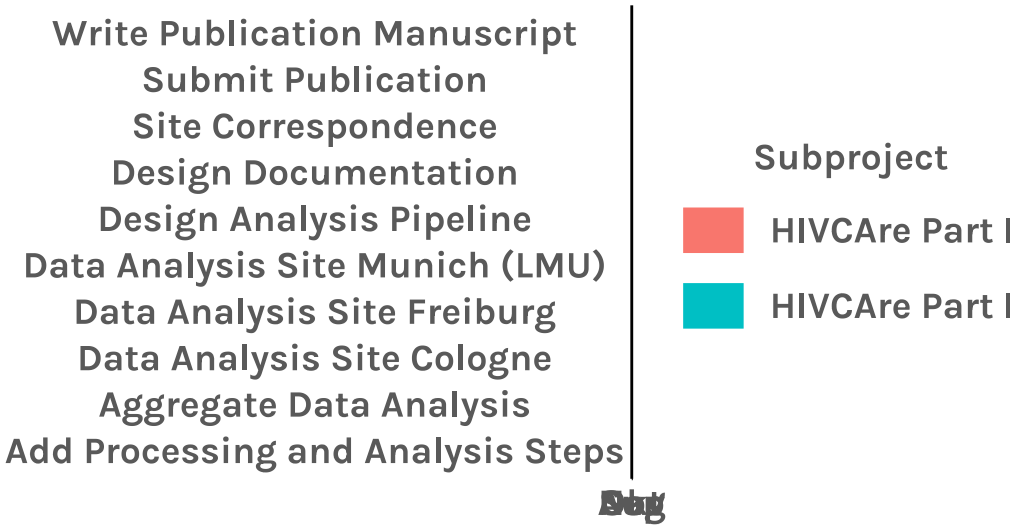
4.6 Meta Data

5 Administration

5.1 Ethics Committee Votes

5.2 Use and Access Request

6 Roadmap


Write Publication Manuscript
Submit Publication
Site Correspondence
Design Documentation
Design Analysis Pipeline
Data Analysis Site Munich (LMU)
Data Analysis Site Freiburg
Data Analysis Site Cologne
Aggregate Data Analysis
Add Processing and Analysis Steps
Subproject
HIVCAre Part I
HIVCAre Part I

7 Documents

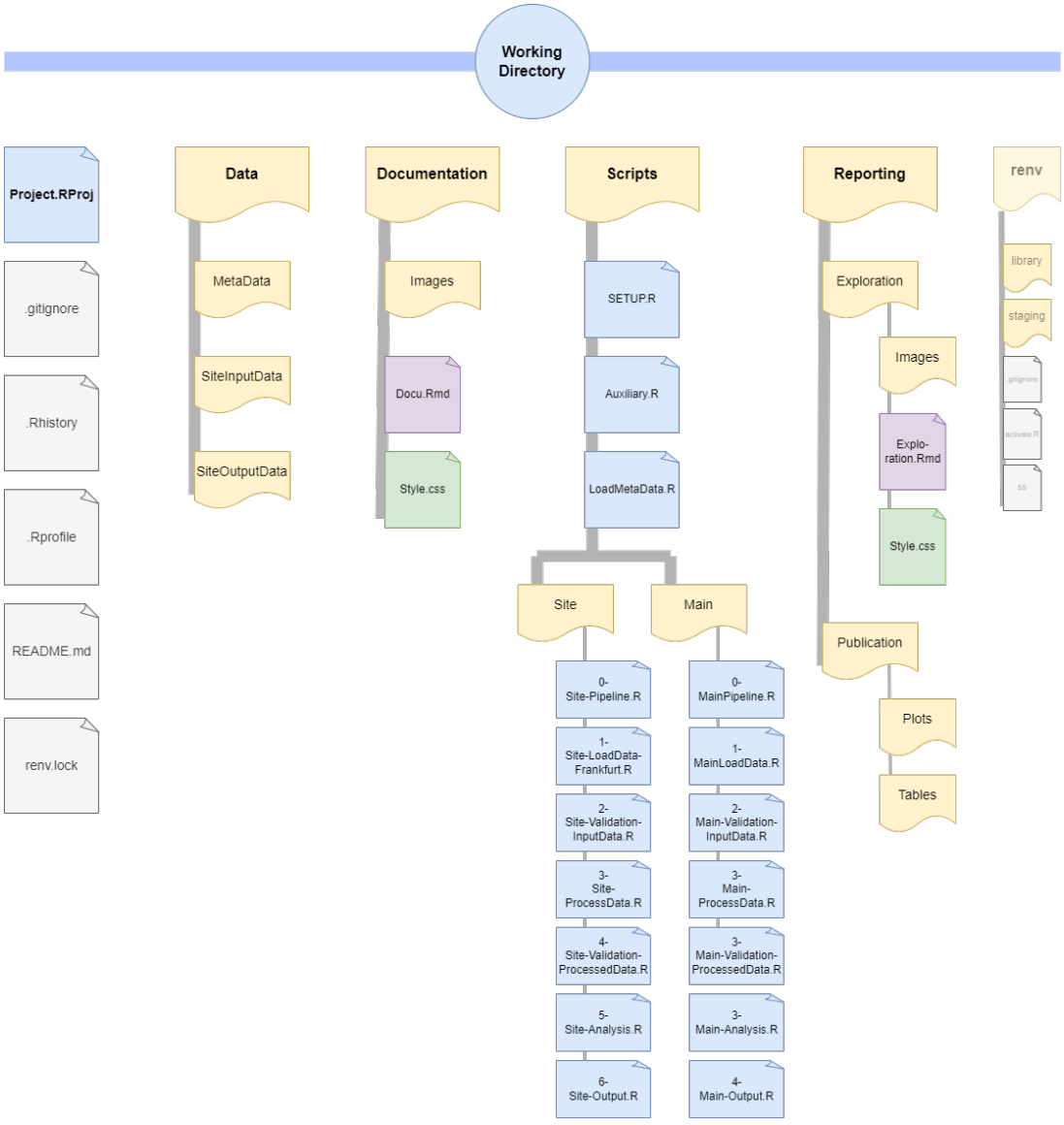
Part III

Technical Documentation

8 General Approach

8.1 GitLab Repository

Flowchart: Gitlab Repository -> Cloning -> Put Data in folder “SiteInputData” -> Run Script (0-SitePipeline.R) ->


Working Directory
Project.RProj
.gitignore
.Rhistory
.Rprofile
README.md
renv.lock
Data
MetaData
SiteInputData
SiteOutputData
Documentation
Images
Docu.Rmd
Style.css
Scripts
SETUP.R
Auxiliary.R
LoadMetaData.R
Site
Main
0-Site-Pipeline.R
1-Site-LoadData-Frankfurt.R
2-Site-Validation-InputData.R
3-Site-ProcessData.R
4-Site-Validation-ProcessedData.R
5-Site-Analysis.R
6-Site-Output.R
0-MainPipeline.R
1-MainLoadData.R
2-Main-Validation-InputData.R
3-Main-ProcessData.R
3-Main-Validation-ProcessedData.R
3-Main-Analysis.R
4-Main-Output.R
Reporting
Exploration
Images
Explo-ration.Rmd
Style.css
Publication
Plots
Tables
renv
library
staging

9 Data Specifications

9.1 Cohort selection

9.2 Required Data Elements

9.3 Harmonized Input Data Model

Attribute Name	Attribute Data Type	Value Format	Value Restrictions
df_Cases			
PatientPseudonym	character		
CasePseudonym	character		
YearOfBirth	integer	9999	[1890 - 2006]
Sex	factor	c	{w, m, u, d, x}
PostalCode	character	99999	
AdmissionDate	date	YYYY-mm-dd	[2005-01-01 - 2022-12-31]
AdmissionAge	integer	99	[18 - 120]
DischargeDate	date	YYYY-mm-dd	[2005-01-01 - 2022-12-31]
DischargeReason	factor	999	{01x, 02x, 03x, 04x, 059, 069, 079, 089, 099, 10
df_CasesICD			
CasePseudonym	character		
DiagnosisType	factor	CC	{HD, ND}
ICDVersion	integer	9999	[1990 - 2023]
ICDCode	character	C99.x	
SecondaryICDCode	character	C99.x	
df_CasesOPS			
CasePseudonym	character		
OPSVersion	integer	9999	[1990 - 2023]
OPSCode	character	9999xx	
OPSDate	date	YYYY-mm-dd	[2005-01-01 - 2022-12-31]

10 Runtime Environment

10.1 renv

10.2 Utilized Packages

10.3 R Environment at Runtime

Part IV

Analysis

Part V

Publications

Publications

Publication Type	Full Title
Published	
Abstract	Epidemiology and Inpatient Care Characteristics of HIV-positive Cancer Patients: Explor
Poster	Epidemiology and Inpatient Care Characteristics of HIV-positive Cancer Patients: Explor
Submitted	
Abstract	Epidemiology and Inpatient Care Characteristics of HIV-positive Cancer Patients: Federa
To be submitted	
Poster	

11 References

Sandve, Geir Kjetil, Anton Nekrutenko, James Taylor, and Eivind Hovig. 2013. "Ten Simple Rules for Reproducible Computational Research." Edited by Philip E. Bourne. *PLoS Computational Biology* 9 (10): e1003285. https://doi.org/10.1371/journal.pcbi.1003285.