RWD86

Heterogeneity in Biomarker Data Collection, Recording and Availability across European Sources of Oncology RWD & Potential Impacts on Pan-EU HTA Assessment

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INTRODUCTION

- The new EU health technology assessment (HTA) regulation aims to streamline access to novel technology across Europe through a unified HTA framework & standardised joint clinical assessment process.[1]
- A key aspect of this new framework is to harmonise the Population, Intervention, Comparator, and Outcome (PICO) scoping process across Europe.
- Oncology treatments are increasingly indicated for populations with specific genetic biomarkers. Therefore, biomarker data will become a crucial and relevant criterion within the PICO scheme for a valid and robust assessment.

OBJECTIVES

- To describe the variation in genetic biomarker data collection, and availability, in oncology populations across European secondary data sources.

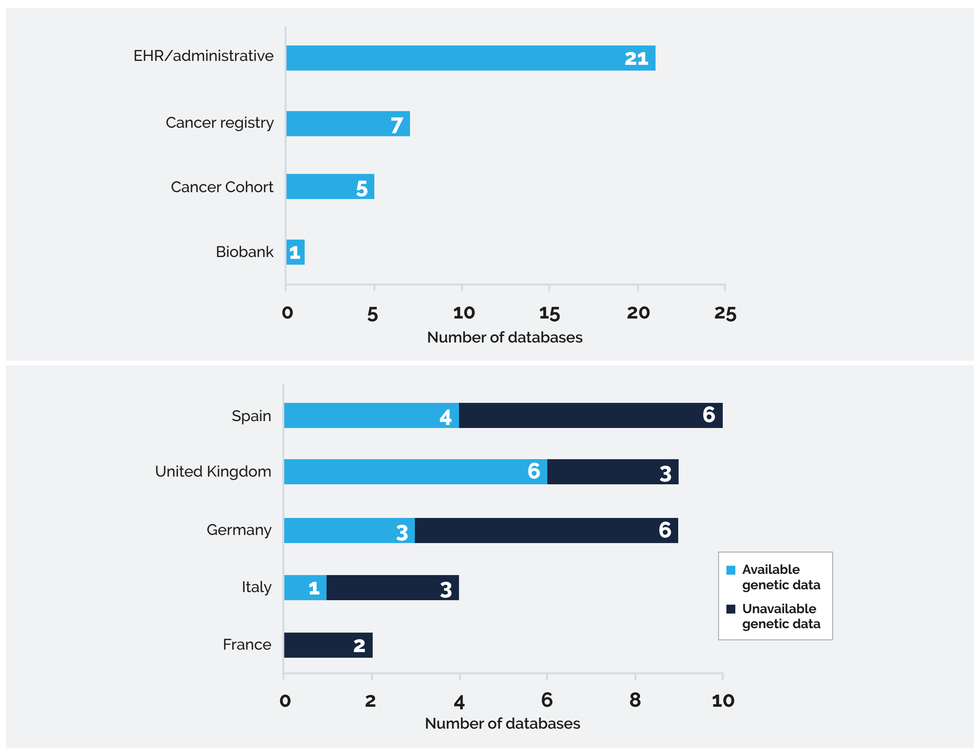
METHODS

- Real-world data sources were identified using a structured search on networks/data listing registries, including
  - Heads of Medicines Agencies-European Medicines Agency (HMA-EMA) catalogues[2]
  - Bridge to Data[3]
  - European Health and Data Evidence Network[4]
- **Inclusion criteria**
  - Geography: databases in UK, Germany, France, Spain, Italy
  - Data type: electronic health records (EHR), electronic medical records (EMR), claims/ administrative database, registries, biobanks
  - Follow-up: longitudinal data collection
  - Coverage: national databases (if not available regional databases were considered)
- **Exclusion criteria**
  - Data type: cross-sectional database or survey, primary care database, chart-review database
  - Databases with only paediatric patients
- **Feasibility assessment:** Administrative information and access details were collected for each identified database from information available online, or, whenever a database was contacted directly, from information gathered via email exchanges or during teleconference calls.
- **Viability assessment:** Details on the availability and granularity of genetic biomarker data as well as patient characteristics, treatment patterns, clinical outcomes, and laboratory assessments for each database were assessed.

RESULTS

- In total, 282 databases were retrieved and initially assessed for relevance. Of these 46 relevant databases were included in the feasibility assessment, and 34 were taken forward for viability assessment (**Figure 1**).
- Out of 34 databases, 14 data sources store, or make available, biomarker data.
- Genetic biomarkers data available in the sources range from whole genome sequencing (e.g., UK biobank) to only a few specific markers (e.g., Scottish Cancer Registry, Big Data Sanitario de Aragón) (**Table 1**).

Figure 1. Number of identified databases by type (upper panel) and country stratified by genetic data availability (lower panel)



Lower panel is stratified by genetic data availability.

RESULTS (CONT)

Table 1. Databases with genetic biomarkers data

COUNTRY	DATABASE NAME	DATABASE TYPE	GENETIC BIOMARKERS
Germany	CRRLP	Registry	ER, HER2, PR
	OncalizerReg	Registry	ALK, BRAF, EGFR, ES, HER2, IgVH, Janus kinase 2 V617F mutation, KRAS, MSI, NRAS, PDL1, PR, ROS1, TP53
	PAN Registry	Registry	No details are available
Italy	MACADAM	Cancer cohort	ACACA, ACE, ADAMTS13 gene full mutation analysis, AGO1, ARRB2, BET1, BCOR (BCL6 corepressor), CALCA, Coccidioides sp DNA, FSHR, HER2 Ag, IGF1, Jo-1 extractable nuclear Ab, MT-CO2, MYCN gene copy number, PCARE, PTP4A1, RAPGEF1, RHCG, STAM, TET2, TPO
Spain	BiGAN	EHR/EMR	BRCA, EGFR
	HUVM	EHR	No details are available
	ICO	Registry	Genetic markers of non-cancer hereditary diseases
	IDIVAL	EHR/EMR	CALR gene exon 9, F2 gene c.20210G>A, F5 gene p.Arg506Gln, IL28B gene associated variant rs12979860, JAK2 gene exon 12, JAK2 gene p.Val617Phe, LCT gene mutations, MTHFR gene c.1298A>C, NPM1 gene mutations, SERPINA1 gene mutations, TPMT gene c.460G>A, TPMT gene c.238G>C, TPMT gene c.719A>G, t(9;22)(q34.1;q11)(ABL1,BCR) e1a2 fusion transcript, t(9;22)(q34.1;q11)(ABL1,BCR) b2a2+b3a2 fusion transcript
UK	NCRAS	Registry	ER, HER2, PR, somatic mutations
	NICR	Registry	No details are available
	SCR	Registry	ER, HER2, PR
	SESCD	Registry	BRCA1, BRCA2, ER, HER2, PR
	UK Biobank	Biobank	Whole genome sequencing, whole exome sequencing, genotyping (800,000 genome-wide variants and imputation to 90 million variants), cancer common variants, common mitochondrial DNA variants, eQTL, NHGRI GWAS catalog, pharmacogenetics/ADME, protein truncating variants, rare variants in cancer predisposition genes, rare coding variants, genome-wide coverage for common variants, genome-wide coverage for low-frequency
	WCISU	Registry	No details are available

Abbreviations: ABL: Abelson; ACACA: acetyl-CoA carboxylase alpha; ACE: angiotensin I converting enzyme; ADME: absorption, distribution, metabolism, and excretion; AGO1: argonaute RISC component 1; ALK: Anaplastic Lymphoma Kinase; ARRB2: arrestin beta 2; BCL: B-cell lymphoma; BCOR: BCL6 corepressor; BCR: breakpoint cluster region protein BET1: Bet1 golgi vesicular membrane trafficking protein; BiGAN: Big Data Sanitario de Aragón; BRAF: B-Raf Proto-Oncogene; BRCA: breast cancer gene; CALCA: calcitonin related polypeptide alpha; CALR: calreticulin CRRLP: Cancer Registry Rhineland-Palatinate; EGFR: Epidermal Growth Factor Receptor; eQTL: expression quantitative trait locus; ER: estrogen receptor; FSHR: follicle stimulating hormone receptor; GWAS: genome-wide association studies; HER2: Human Epidermal Growth Factor Receptor 2; HUVM: Hospital Universitario Virgen Macarena; ICO: Institut Català d'Oncologia; IDIVAL: Instituto de Investigación Marqués de Valdecilla; IGF: insulin like growth factor; IgVH: Immunoglobulin Variable Heavy Chain; IL: interleukine JAK: Janus kinases; KRAS: KRAS Proto-Oncogene; LCT: lactase MACADAM: Mesothelioma Clinical Data Platform; MSI: Microsatellite Instability; MT-CO2: mitochondrially encoded cytochrome c oxidase II; MTHFR: methylenetetrahydrofolate reductase; NCRAS: National Cancer Registration and Analysis Service; NHGRI: National Human Genome Research Institute NICR: Northern Ireland Cancer Registry; NPM: nucleophosmin NRAS: NRAS Proto-Oncogene; PCARE: photoreceptor cilium actin regulator; PDL1: Programmed Death-Ligand 1; PR: progesterone receptor; PTP4A1: protein tyrosine phosphatase 4A1; PTP53: Tumor Protein P53; RAPGEF1: Rap guanine nucleotide exchange factor 1; RHCG: Rh family C glycoprotein; ROS1: ROS Proto-Oncogene 1; SCR: Scottish Cancer Registry; SERPINA1: Serine protease inhibitor alpha-1 antitrypsin; SESCD: South East Scotland Cancer Database; STAM: signal transducing adaptor molecule; TET2: tet methylcytosine dioxygenase 2; TPMT: thiopurine S-methyltransferase; TPO: thyroid peroxidase; WCISU:Welsh Cancer Intelligence & Surveillance Unit.

CONCLUSIONS

- Several of the data sources did not store, or make available, biomarker data.
- Where biomarker data was available it was varied across the sources.
- The heterogeneity of genetic biomarker data — such as availability, type, and number of biomarkers, technologies used, and protocols followed — in data sources for secondary use, presents challenges for defining aligned PICO definitions in multi-country. This is particularly important in the context of a pan-EU regulatory process.
- The efficiency, and alignment, of generated evidence would be improved through alignment of biomarker data collection, recording and reporting across EU sources of oncology real-world data.

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DISCLOSURES

The authors are employees of OPEN Health.

ACKNOWLEDGEMENTS
We would like to thank members of Scientific Office for their support.

Presented at: ISPOR Europe 2024

Sponsored by OPEN Health's Scientific Office