

Clinical Exposome of Patient-Reported Outcomes for Patients with Metastatic Breast Cancer

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INTRODUCTION

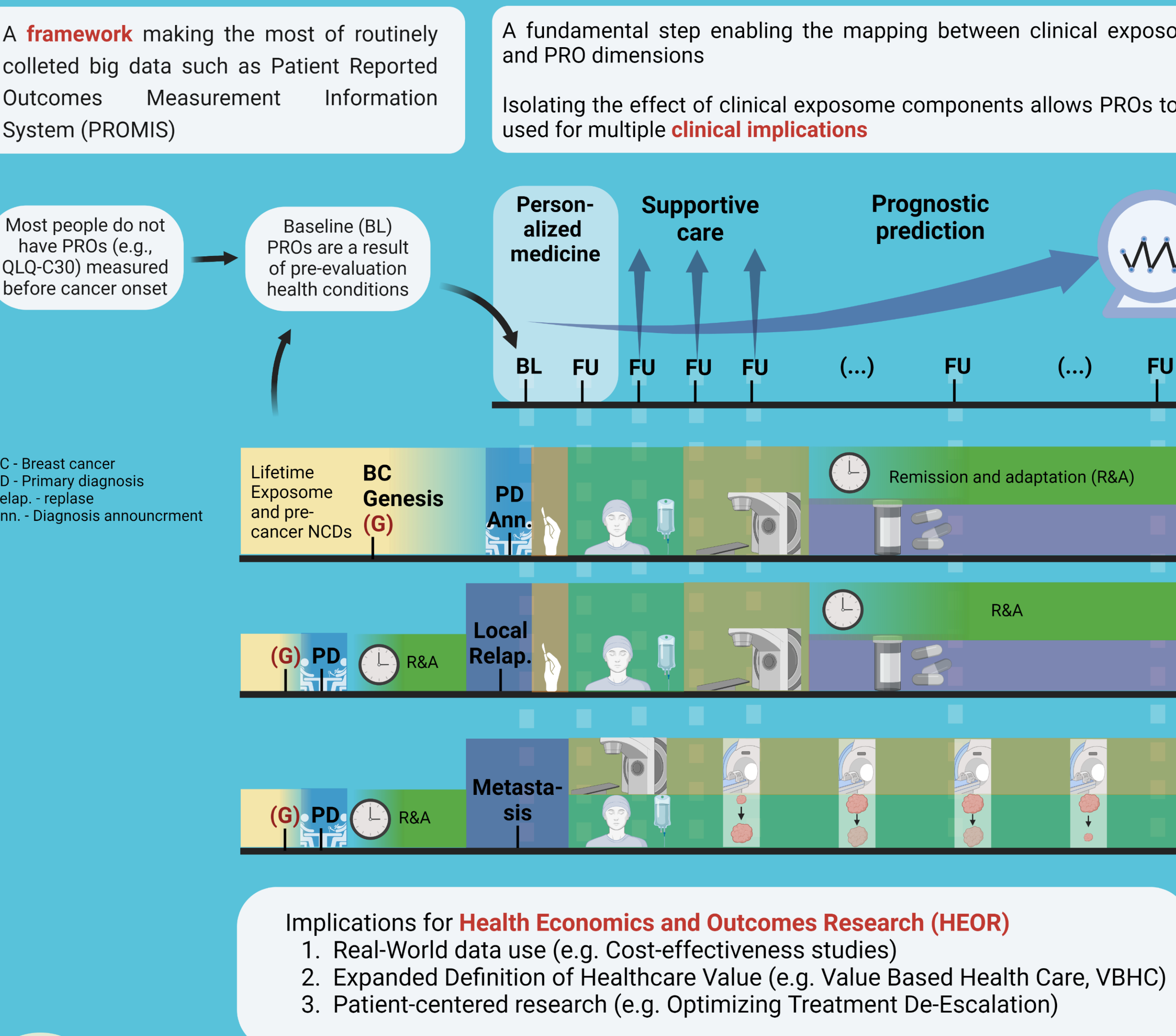
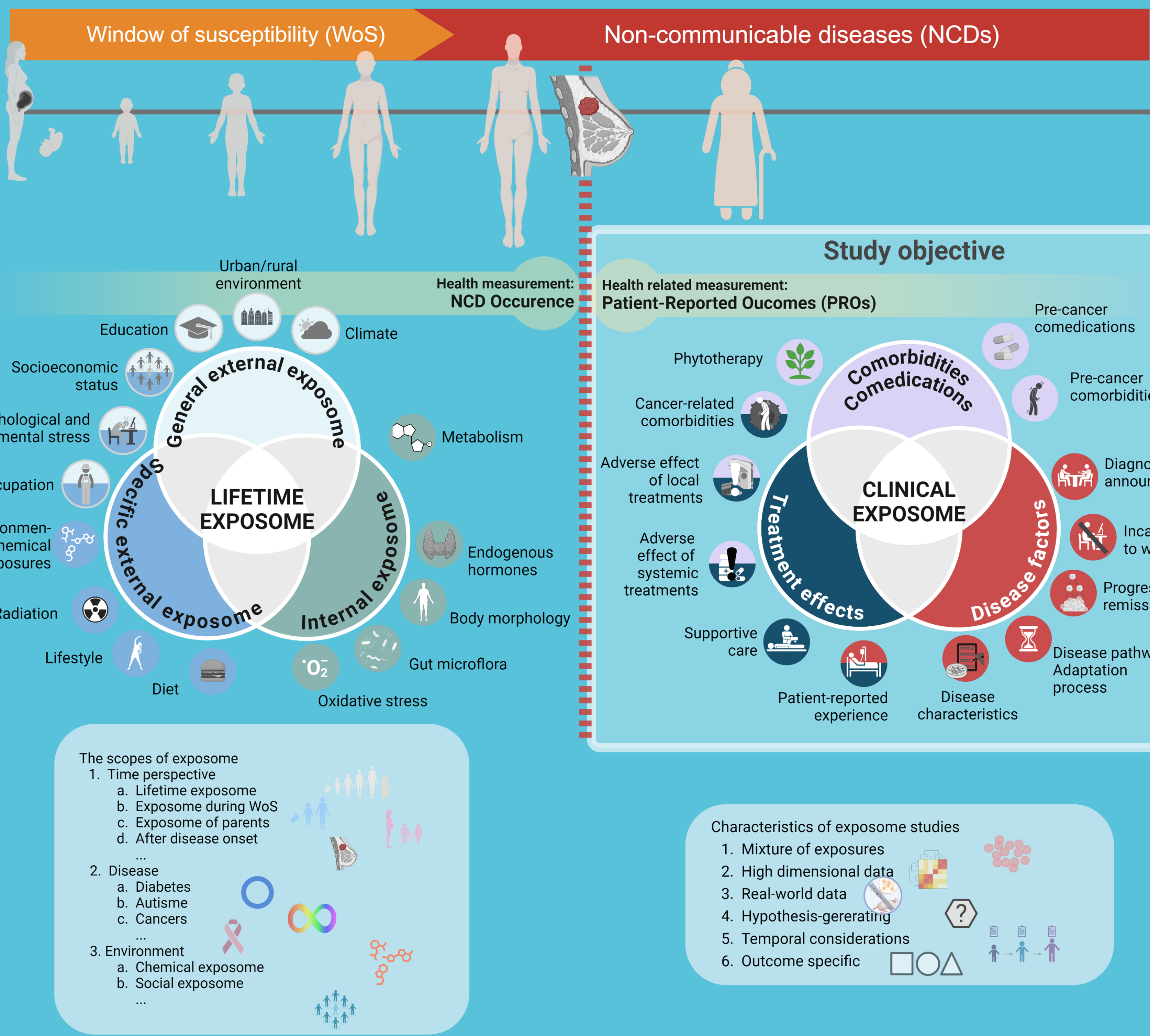
The exposome refers to all exposures to which an individual is subjected through out lifetime. The most immediate sphere for patients with severe conditions such as metastatic breast cancer is likely to be the clinical than the environmental exposome. Recently, clinical research data and Electronic Health Records (EHRs) have become a potential source for tracing the clinical exposome. Since Patient-Reported Outcomes (PROs) are sensitive to the exposome, this conceptual study examines the methodological implication of conducting clinical exposome research on PROs.

METHODS

We performed a scoping review along with an analysis of real-world clinical data. We adapted exposome methods to clinical information by focusing on hypothesis-driven processes within high-dimensional data and on generating new insights into how specific clinical exposures are mapped to specific PRO dimensions.

RESULTS

Unstructured information in electronic Clinical Research Forms (eCRFs) and EHRs including heterogeneous entries (e.g. misspellings, synonyms, commercial and generic names, deviations in expressions) will be refined into specific structured variables (e.g. co-medications, family history or occasional symptoms) using large language models (LLMs). Structured data in eCRFs, such as disease characteristics, treatments, comorbidities, critical clinical events, psychometric measures, and medical procedures in EHRs, will be used directly and in combination to describe the clinical patterns of the disease and treatment pathway. A minimum of 200 longitudinal clinical variables times the number of repeated measures will be used. The exposome-wide association study (ExWAS) will then screen each clinical exposure with individual PRO questions and dimensions. We will use cross-validated Lasso regression models to assess how a set of clinical variables affect PROs.



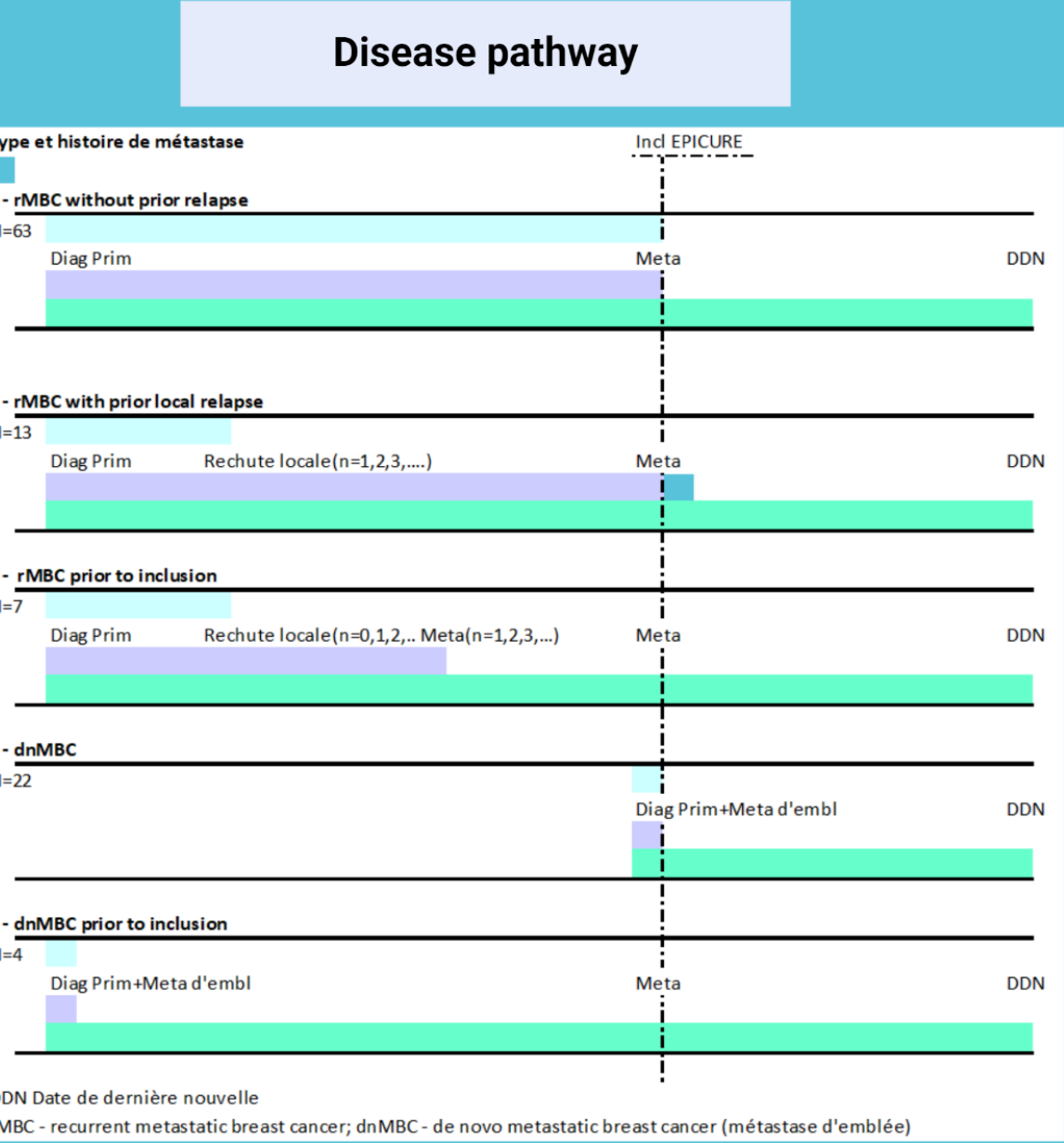
EPIPURE Cohort
ICO Comprehensive Cancer Centre, Saint-Herblain (Nantes), France

- Metastatic breast cancer
- High-dimensional and heterogeneous data
- Multiple scientific objectives including
 - a. mechanism of treatment resistance
 - b. cancer management
 - c. PROs research
 - d. omics sciences
 - e. internal and external exposome
- First dataset for analyzing more than 6000 variables retrieved from 46 sub-datasets

Structured variables based on needs analysis

Large Language Models

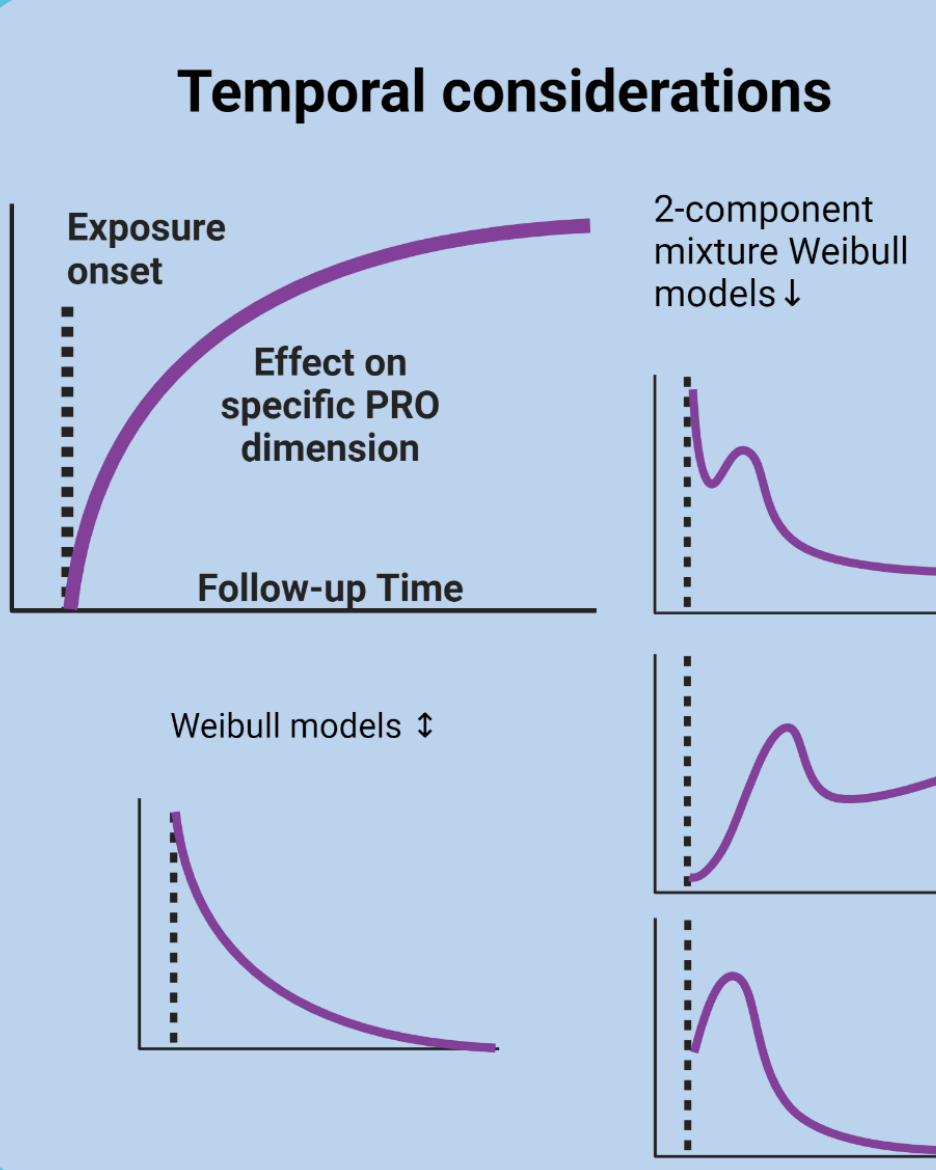
Heterogeneous entries in EHRs



Comorbidities	Comedications	Chemotherapy	Family Hist. of cancer
<p>(Examples of free text entries in French)</p> <ul style="list-style-type: none">DIABETEDIABETE DE TYPE IDIABETE DE TYPE IIDIARRHÉE CHRONIQUEDISCOPATHIEDYSURIEDiabète de type IIDyslipidémieEndométrioseEMBOLE PULMONAIREEXTRACTION GÉNÉRALEFIBROSEFAUSSE COUCHEFIBROMYALGIEFractureGYNECOLOGIEHERNIE OMBILICALEHTAHYPERCHOLESTÉROLÉMIÉHYPERHYDROÏDEHYPERHYPOTENSIONHYSTERECTOMIEHYSTEROSCOPIEHYSTEROSALPINGOGRAPHIEHyperthyroïdieHypothyroïdieHystérectomieIVG	<p>(Examples of free text entries in French)</p> <ul style="list-style-type: none">3 EC 12TAXOL3 FEC + 3 TAXOTERE3 FEC 1003 FEC 100 DOCE TAXEL3 FEC 100 + 3 TAXOTERE3 FEC 3 DOCE TAXEL3 TAXOTERE3 EC 1006 TAXOL AVASTIN6 TAXOTERETRASTUZUMABPERTUZUMAB8 TAXOLHEBDOMADAIREABBIE M12 914 (TAXOL+CARBO)ACAC PACLITAXELADRIAMYCINEADRIAMYCINECYCLOPHOSPHAMIDEADRIAMYCINETRAMADOL PARACETAMOL31 SMO 1000TRAMADOL 1000TRIMETHYLPHTHOLICINOLTRIMETHYLPHTHOLICINOLTRIMETHYLPHTHOLICINOL	<p>(Examples of free text entries in French)</p> <ul style="list-style-type: none">3 EC 12TAXOL3 FEC + 3 TAXOTERE3 FEC 1003 FEC 100 DOCE TAXEL3 FEC 100 + 3 TAXOTERE3 FEC 3 DOCE TAXEL3 TAXOTERE3 EC 1006 TAXOL AVASTIN6 TAXOTERETRASTUZUMABPERTUZUMAB8 TAXOLHEBDOMADAIREABBIE M12 914 (TAXOL+CARBO)ACAC PACLITAXELADRIAMYCINEADRIAMYCINECYCLOPHOSPHAMIDEADRIAMYCINETRAMADOL PARACETAMOL31 SMO 1000TRAMADOL 1000TRIMETHYLPHTHOLICINOLTRIMETHYLPHTHOLICINOLTRIMETHYLPHTHOLICINOL	<p>(Examples of free text entries in French)</p> <ul style="list-style-type: none">AUCUN ATCDBRONCHIQUECANCER EN LIEN AVEC TABACCANCER LIE A LAMIANTECANCER NON PRECISECAVITE BUCCALEPHARYNX PARTIES AUTR.CEREBRALCOL UTERINCOLONCOLON GRAND PEREMATERNELCOLON ONCLEPATERNELENCEPHALEESTOMACFOIEFOIE ET VOIES BILIAIRESINTRAPEATIQUESFRERE - MELANOME 2008FRERE OESOPHAGEINTESTIN GRELEKLANGUELEUCEMIE

Mapping from Clinical Exposome to PRO dimensions

Clinical exposome components :	possible effects on:	PRO dimensions :
Diagnosis announcement	EF (...)	AP - Appetite loss
Conservative Surgery	EF, PA, FA, CF (...)	BI - Body Image
Mastectomy	BI, BS, SF (...)	BS - Breast Symptoms
Chemotherapy protocol A protocol B	FA, PF, NV (...)	CF - Cognitive Functioning
Imaging progression report	EM, SF (...)	CO - Constipation
Imaging remission report	EM, FU (...)	DI - Diarrhoea
Hormonotherapy	ST (...)	EF - Emotional Functioning
Phytotherapy	CO, FA (...)	FA - Fatigue
Diabetes	AP, CO, DI, PF (...)	FU - Future perspective
Tendinopathy	PF, PA (...)	HL - Hair Loss
Rheumatoid arthritis	PF, PA, SF (...)	NV - Nausea and Vomiting
Parkinson's disease	PF, SF, CF (...)	PA - Pain
Chronic respiratory disease	PF, SF, CF (...)	PF - Physical Functioning
Family history of cancer	EM, FU (...)	SF - Social Functioning
35 years of breast cancer survival since PD	EF, SF, FU (...)	ST - Systemic side effects
Triple negative breast cancer	EM, FU (...)	(...)
(...)	(...)	(...)



Statistical methods for clinical exposome variables selection and analysis

ExWAS - Exposome-wide association study
ENET - Elastic-Net
DLNM - Distributed Lag Non-linear Models
sPLS - Sparse Partial Least-Squares Regression
DSA - Deletion-Substitution-Addition Algorithm
NPLS - Sparse N-Way Partial Least-Square
BKM - Bayesian Kernel Machine
Jugement criteria:
Sensitivity
False discovery rate
(...)

CONCLUSION The clinical exposome framework is a critical component for both the patient-centered care and research on PROs. It helps map patient clinical exposures to PROs dimension and isolate their effects to specific dimensions. This serves the value-based care ultimately.

CONTACT INFORMATION

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