

VENDREDI 4 OCTOBRE 2024  
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17E COLLOQUE DU CANCÉROPÔLE IDF

# VIEILLISSEMENT ET CANCERS :

DE LA RECHERCHE FONDAMENTALE  
À LA RECHERCHE TRANSLATIONNELLE  
ET APPLICATIONS CLINIQUES POUR L'AVENIR

## Apport des données de vie réelle pour la recherche clinique en oncogériatrie

Florence Canoui-Poitaine  
APHP, Henri-Mondor  
UPEC, Faculté de Santé  
Inserm, Equipe CEpiA

[CEpiA - Clinical Epidemiology and Ageing](#)



# Naissance de la notion de RWD et RWE



Naissance de  
Real-World Data /  
Real-World Evidence

# Naissance de la notion de RWD et RWE



FDA STATEMENT

## Statement from FDA Commissioner Scott Gottlieb, M.D., on FDA's new strategic framework to advance use of real-world evidence to support development of drugs and biologics



“The health care system is integrating more effective ways to leverage **electronic tools** to gather and use vast amounts of health-related data. These tools offer new opportunities to use data collected during the routine care of patients to advance medical care. **Leveraging such data – typically called real-world data (RWD) - to improve regulatory decisions is a key strategic priority for the FDA”**

These data may be derived from a diverse array of sources, such as **electronic health records (EHR), medical claims, product and disease registries, laboratory test results** and even cutting-edge **technology paired with consumer mobile devices**.

These data are being used to develop information and **real-world evidence (RWE) that can better inform regulatory decisions**.

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## Essai thérapeutique idéal





SPECIALTIES ▼



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PUBLICATIONS

ORIGINAL ARTICLE

# A Twen Expose

**Authors:** Marluc  
Herbst, M.D. /

**Published April**  
**VOL. 298 NO. 1**

## Abstract

### ABSTRACT

To assess the long-term effects of diethylstilbestrol we conducted a health survey among 693 mothers who had taken the drug during pregnancy and a comparable group of 668 who had not. These women had participated in a study during 1951–52 to evaluate the drug. There were 32 (4.6 per cent) breast cancers among the 693 exposed and 21 (3.1 per cent) among the 668 unexposed, but the difference was not statistically significant ( $P = 0.16$ ). No statistically significant differences occurred between the groups in any of the other categories of disease. The occurrence of breast cancer in both groups was compared to the Connecticut State Tumor Registry for 1963–65. Compared to the registry data, a significantly ( $P < 0.01$ ) higher incidence of breast cancer occurred in both the exposed and unexposed groups at ages over 50. The reason for this increase is not known, but effects linked to the selection of mothers participating in the original clinical study cannot be excluded. (N Engl J Med 298:763–767, 1978)

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# Women Pregnancy

Hubby, Ph.D., and Arth

81403





# Type of postmenopausal hormone use and risk of breast cancer: 12-year follow-up from the Nurses' Health Study

Graham A. Colditz, Meir J. Stampfer, Walter C. Willett,  
David J. Hunter, JoAnn E. Manson, Charles H. Hennekens,  
Bernard A. Rosner, and Frank E. Speizer

*(Received 9 April 1992; accepted in revised form 16 June 1992)*

We prospectively examined the use of hormone replacement therapy in relation to breast cancer incidence in a cohort of women 30 to 55 years of age in 1976. During 12 years of follow-up (480,665 person-years) among postmenopausal women, 1,050 incident cases of breast cancer were documented. Overall, past users of replacement estrogen were not at increased risk. After adjustment for established risk factors, type of menopause, age at menopause, and current age, the rate ratio (RR) was 0.91, 95 percent confidence interval (CI) = 0.78-1.07. The risk of breast cancer was elevated significantly among current users (RR = 1.33, CI = 1.12-1.57); after

## ORIGINAL REPORT

# Benfluorex and valvular heart disease: a cohort study of a million people with diabetes mellitus

Alain Weill<sup>1\*</sup>, Michel Païta<sup>1</sup>, Philippe Tuppin<sup>1</sup>, Jean-Paul Fagot<sup>1</sup>, Anke Neumann<sup>1</sup>, Dominique Simon<sup>2,3</sup>, Philippe Ricordeau<sup>1</sup>, Jean-Louis Montastruc<sup>4</sup> and Hubert Allemand<sup>5</sup>

<sup>1</sup>*Direction de la Stratégie, des Études et des Statistiques, Caisse Nationale de l'Assurance Maladie, Paris, France*

<sup>2</sup>*Service de Diabétologie, Groupe Hospitalier Pitié Salpêtrière, Paris, France*

<sup>3</sup>*Centre de recherche en Épidémiologie et Santé des Populations, INSERM Villejuif, France*

<sup>4</sup>*Service de Pharmacologie Clinique, Unité de Pharmacopépidémiologie (EA 3696 et INSERM) Centre Hospitalier Universitaire et Faculté de Médecine de Toulouse, Toulouse, France*

<sup>5</sup>*Direction générale, Caisse Nationale de l'Assurance Maladie, Paris, France*

## ABSTRACT

**Purpose** To evaluate and quantify in diabetic patients treated with benfluorex in France, a fenfluramine-derived product, a possible increase in risk of valvular heart disease, previously suggested by several published case reports.

**Methods** This was a French comparative cohort study using data from two large national linked databases, health insurance system (SNIIRAM) and hospitalization (PMSI). Patients aged 40–69 years with reimbursement for oral antidiabetic and/or insulin in 2006 were eligible. Exposed patients were defined as patients with at least one benfluorex reimbursement in 2006. Selected admission diagnoses of interest in 2007 and 2008 PMSI databases were valvular insufficiency for any cause, mitral insufficiency, aortic insufficiency, and valvular replacement surgery with cardiopulmonary bypass. Relative risks (RR) were adjusted on gender, age, and history of chronic cardiovascular disease.

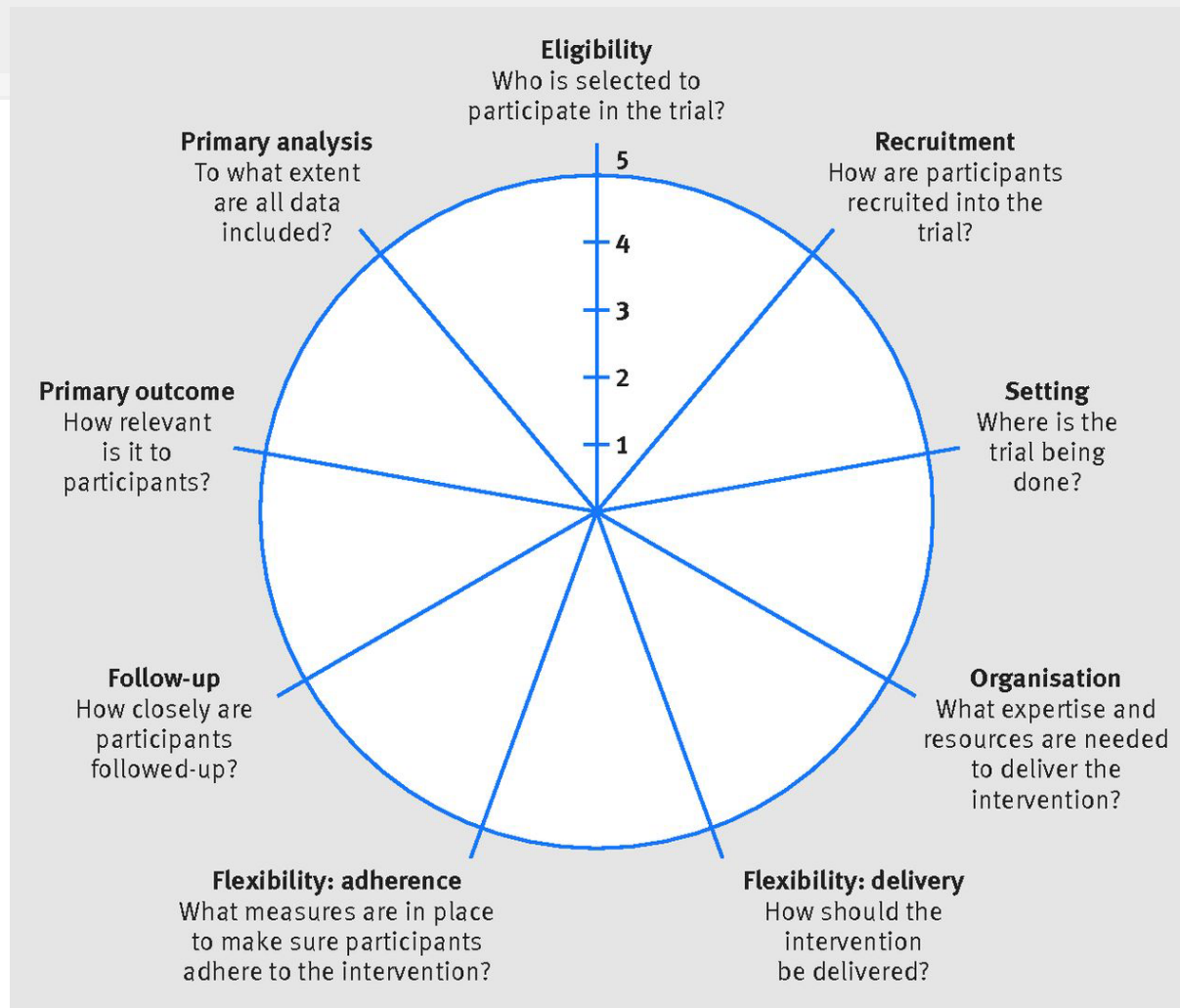
**Results** A total of 1 048 173 diabetic patients were included, with 43 044 (4.1%) exposed to benfluorex. The risk of hospitalization in 2007 and 2008 for any cardiac valvular insufficiency was higher in the benfluorex group: crude RR = 2.9 [95% confidence interval 2.2–3.7] and adjusted RR = 3.1 [2.4–4.0], with a lower risk for patients with lower cumulative dose of benfluorex. Adjusted RR for mitral insufficiency and aortic insufficiency admissions were 2.5 [1.9–3.7] and 4.4 [3.0–6.6], respectively. Adjusted RR for valvular replacement surgery was 3.9 [2.6–6.1].

**Conclusions** Benfluorex in diabetic patients was significantly associated with hospitalization for valvular heart disease in the 2 years following benfluorex exposure. Linkage between SNIIRAM and PMSI databases is in France a valuable tool to quantify the risk of serious adverse drug reactions. Copyright © 2010 John Wiley & Sons, Ltd.

KEY WORDS — benfluorex; valvular heart disease; adverse effects; health insurance system; reimbursement databases; pharmacoepidemiology

Received 14 April 2010; Revised 25 June 2010; Accepted 4 August 2010

# The PRagmatic-Explanatory Continuum Indicator Summary 2 (PRECIS-2) wheel.



Kirsty Loudon et al. BMJ 2015;350:bmj.h2147



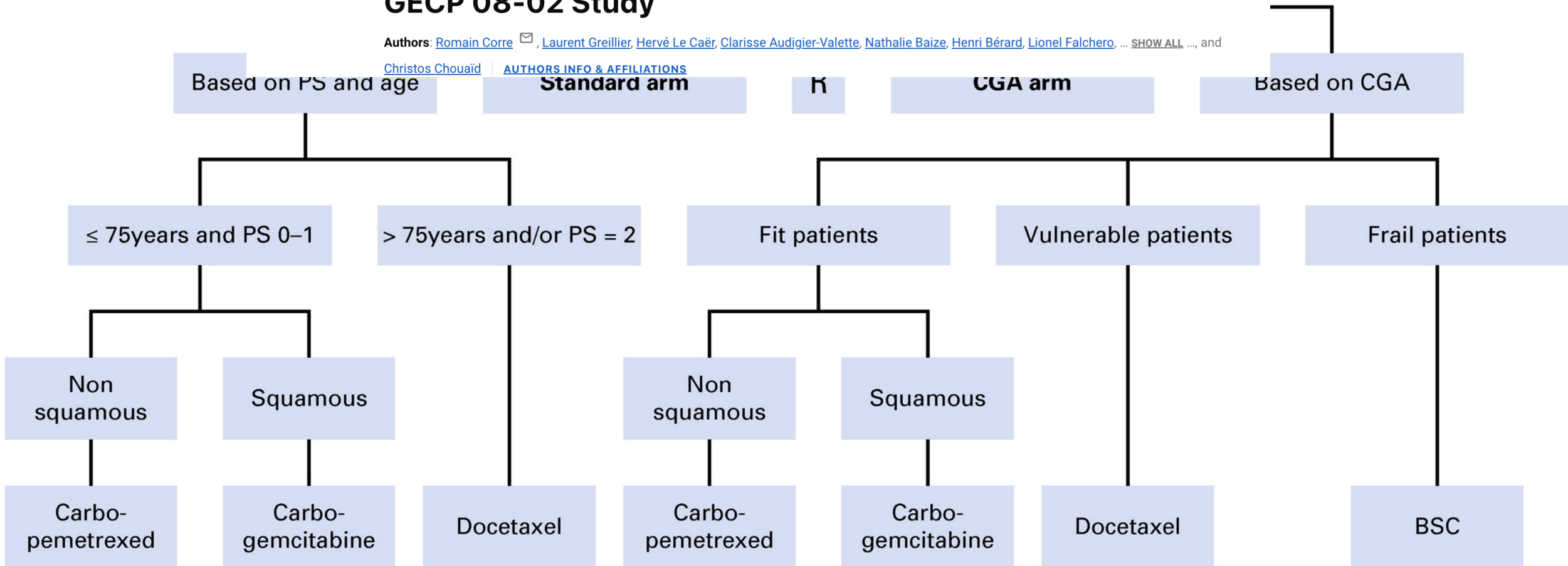
NSCLC > 70 years

PARTIAL ACCESS | ORIGINAL REPORTS | February 16, 2016



# Use of a Comprehensive Geriatric Assessment for the Management of Elderly Patients With Advanced Non-Small-Cell Lung Cancer: The Phase III Randomized ESOGIA-GFPC-GECP 08-02 Study

Authors: [Romain Corre](#), [Laurent Greillier](#), [Hervé Le Caër](#), [Clarisse Audigier-Valette](#), [Nathalie Baize](#), [Henri Bérard](#), [Lionel Falchero](#), ... [SHOW ALL](#) ..., and [Christos Chouaid](#) | [AUTHORS INFO & AFFILIATIONS](#)



SUBMITTED ABSTRACTS | BREAST CANCER, EARLY STAGE · Volume 25, Supplement 4, IV108, September 2014 · [Open Archive](#)

# Aster 7oS Unicancer Phase III Trial : Adjuvant Treatment for Women Over 70 with Luminal Breast Cancer

[C. Dubot](#)<sup>1</sup> · [Y. Tazi](#)<sup>2</sup> · [E. Bourbouloux](#)<sup>3</sup> · ... · [C. Orsini](#)<sup>18</sup> · [F. Bonnetain](#)<sup>19</sup> · [E. Brain](#)<sup>1</sup>... [Show more](#)

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## ABSTRACT

**Background:** Benefit of the additional adjuvant chemotherapy (CT) compared with hormonal therapy alone (HT) remains debated for women >70 with ER+ HER2- breast cancer (BC) and aggressive characteristics. This trial compares the impact of both strategies on overall survival (OS).

**Trial design:** Following surgery, ~2,000 patients (Pts) will have a Genomic Grade (GG) performed centrally on FFPE specimens by RT-PCR. Those with a high risk defined as high or equivocal GG will be randomized to HT alone vs CT + HT. Pts with a low GG will be followed as an observational cohort. OS (all deaths) is the primary endpoint. Secondary objectives include competing events, cost-effectiveness and Q-TWiST analysis, geriatric dimension, willingness and health-related quality of life including specific ELD15. Translational research will focus on prognostic biomarkers and

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Clinical Study | [Open access](#) | Published: 14 April 2015

# The impact of comprehensive geriatric assessment interventions on tolerance to chemotherapy in older people

[T Kalsi](#) , [G Babic-Illman](#), [P J Ross](#), [N R Maisey](#), [S Hughes](#), [P Fields](#), [F C Martin](#), [Y Wang](#) & [D Harari](#)

[British Journal of Cancer](#) **112**, 1435–1444 (2015) | [Cite this article](#)

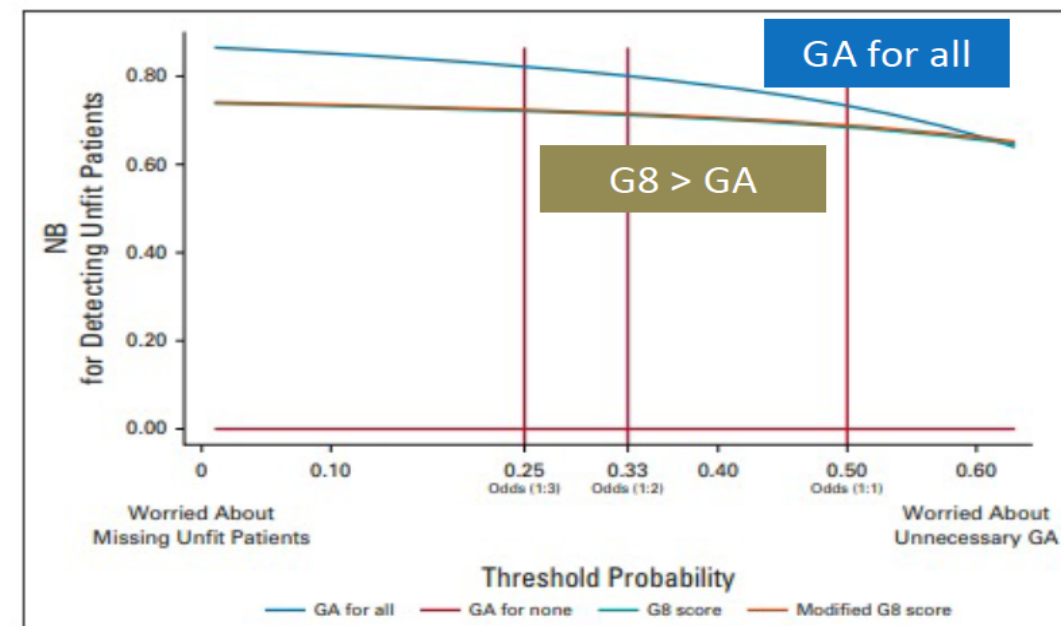
**6555** Accesses | **201** Citations | **67** Altmetric | [Metrics](#)



# ELCAPA Cohort Study 8,000 older patients with cancer (82 years)



Prospective Cohort



GA: geriatric assessment

- 20 publications – 3 J Clin Oncol
- 6 PhD (3 ongoing)
- Ancillary Studies

González Serrano A, et al . A Two-Step Frailty Assessment Strategy in Older Patients With Solid Tumors: A Decision Curve Analysis. J Clin Oncol. 2023 (CEpiA members)



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Journal of Clinical Oncology®  
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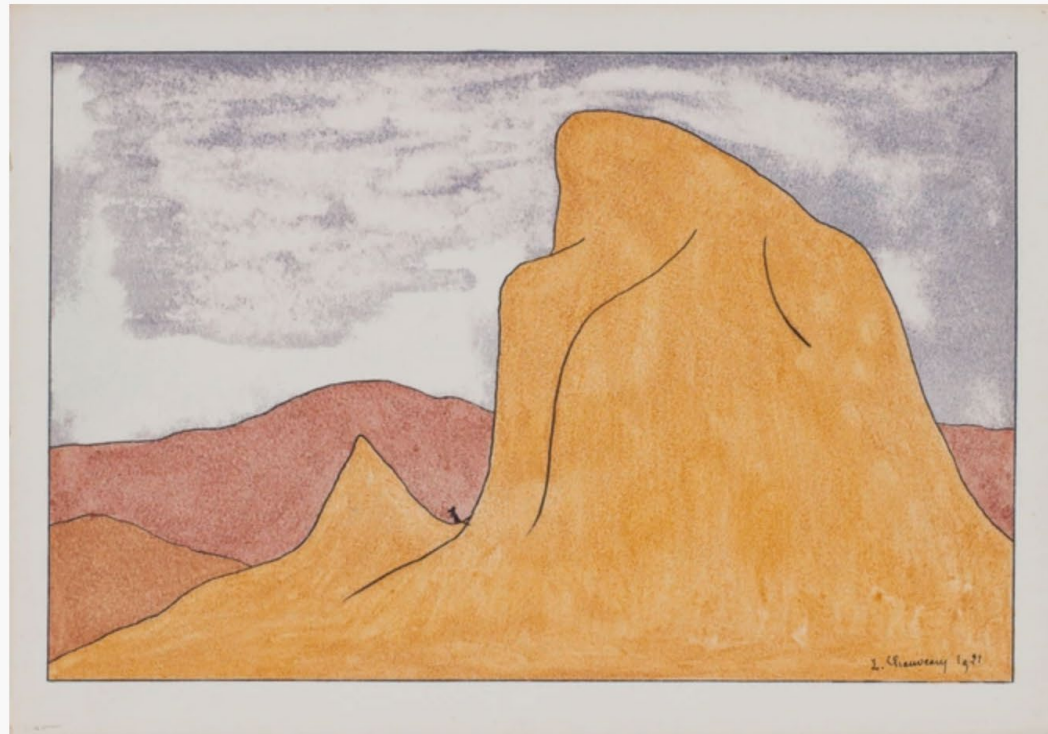


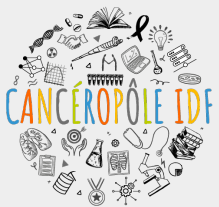
# PALOMAGE, a French real-world cohort of elderly women beyond age 70 with advanced breast cancer receiving palbociclib: Baseline characteristics and safety evaluation.

**Authors:** [Philippe Caillet](#), [Marina Pulido](#), [Etienne Brain](#), [Claire Falandry](#), [Isabelle Desmoulins](#), [Djamel Ghebriou](#), [Pierre-Louis Soubeyran](#), [Elena Paillaud](#), [Nada Rifi](#), [Jean Michel Vauthier](#), [Louis Tassy](#), and [Elisabeth Carola](#) | [AUTHORS INFO & AFFILIATIONS](#)

**Publication:** Journal of Clinical Oncology • [Volume 39, Number 15 suppl](#) • [https://doi.org/10.1200/JCO.2021.39.15\\_suppl.1012](https://doi.org/10.1200/JCO.2021.39.15_suppl.1012)

## Fables de La Fontaine : La Montagne qui accouche d'une souris





25 July 2024  
EMA/CHMP/ICH/295401/2023  
Committee for Medicinal Products for Human Use

ICH reflection paper on pursuing opportunities for  
harmonisation in using real-world data to generate real-  
world evidence, with a focus on effectiveness of  
medicines

on safety and effectiveness,<sup>1,2</sup> other approaches including the use of RWD can generate evidence suitable for regulatory decision-making, e.g. to ascertain endpoints in point-of-care RCTs, or serve as a comparator arm in an externally controlled trial (including historically controlled trials) [US Food and Drug Administration (FDA, United States), Framework for FDA's Real-World Evidence Program (2018)]. RWD are also frequently used in non-interventional studies [FDA, United, States guidance on Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products (2023)], for example, to analyse the utilisation of an authorised medicine in routine medical practice, and to generate evidence that supports regulatory decisions on (long-term) post-marketing safety and effectiveness of medicines [Jonker et al., 2022; Flynn et al., 2022]. In addition, RWD can be used to better understand current treatment patterns, co-morbidities, and disease prognosis.

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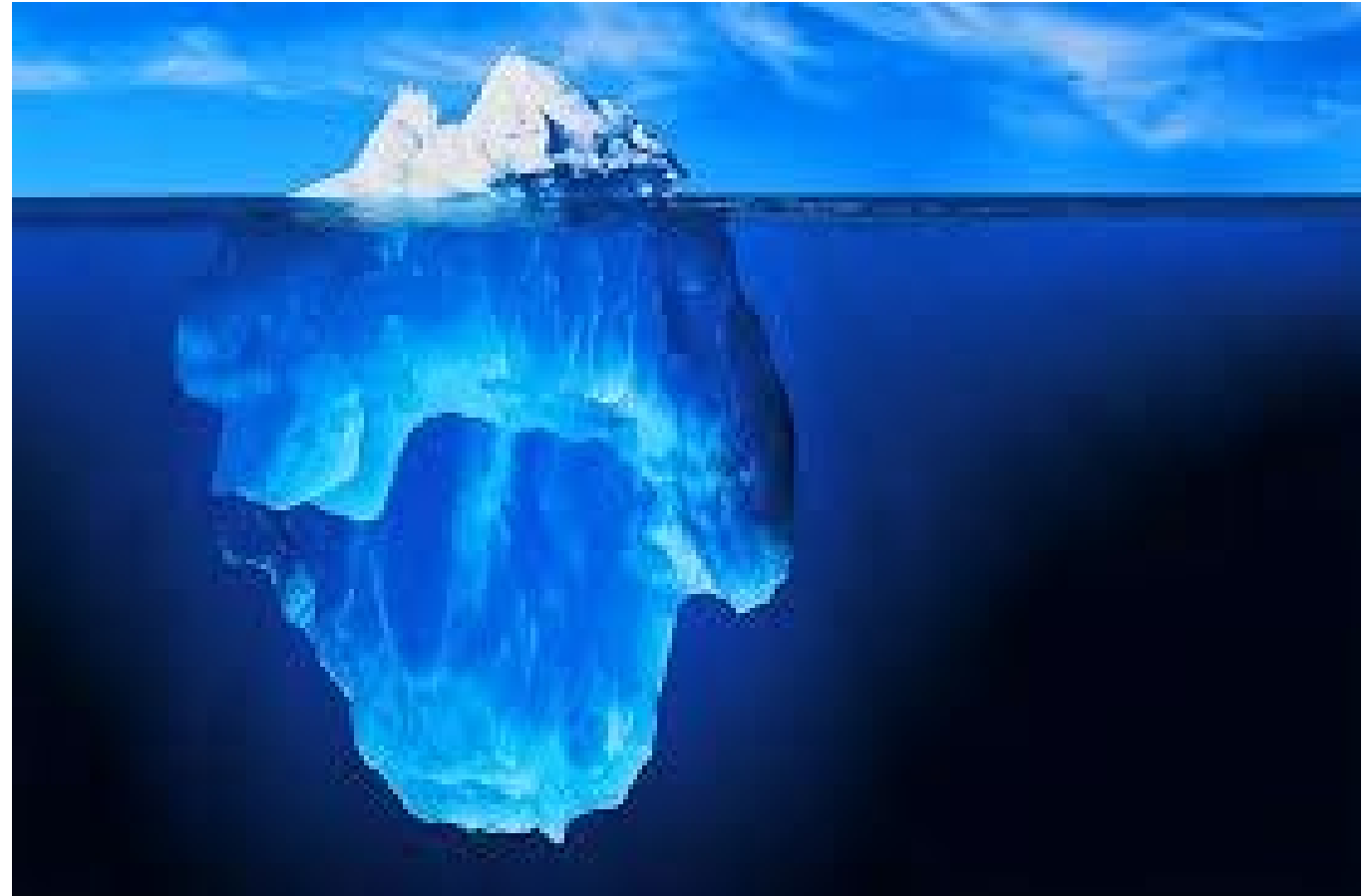
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## Essai thérapeutique idéal



Essai thérapeutique pragmatique      Remboursements de soins

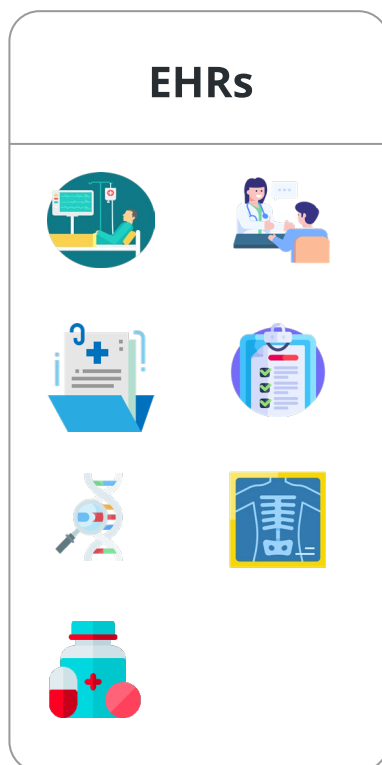
## Registres de traitements ou populationnels

## Cohortes

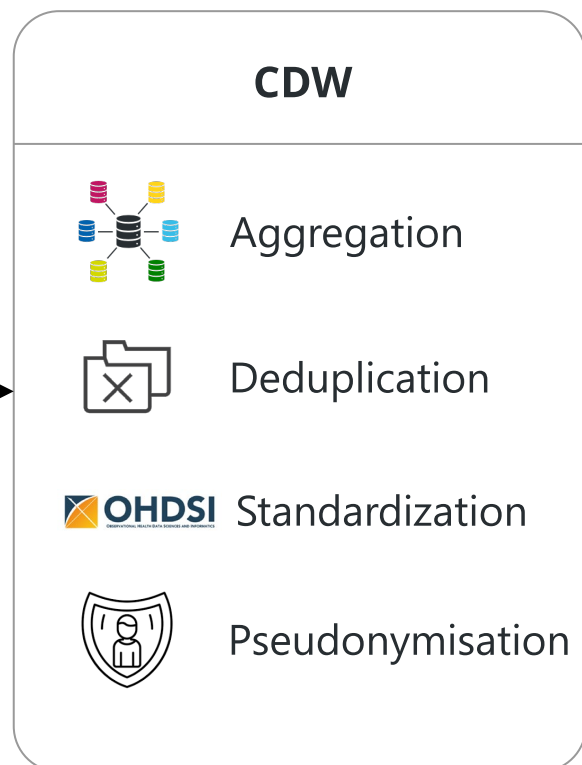
## Séjours hospitaliers

## Entrepôts de données de santé

## 1 - Collection



## 2 - Transformation



## 3 – Use cases

Scientific research +++

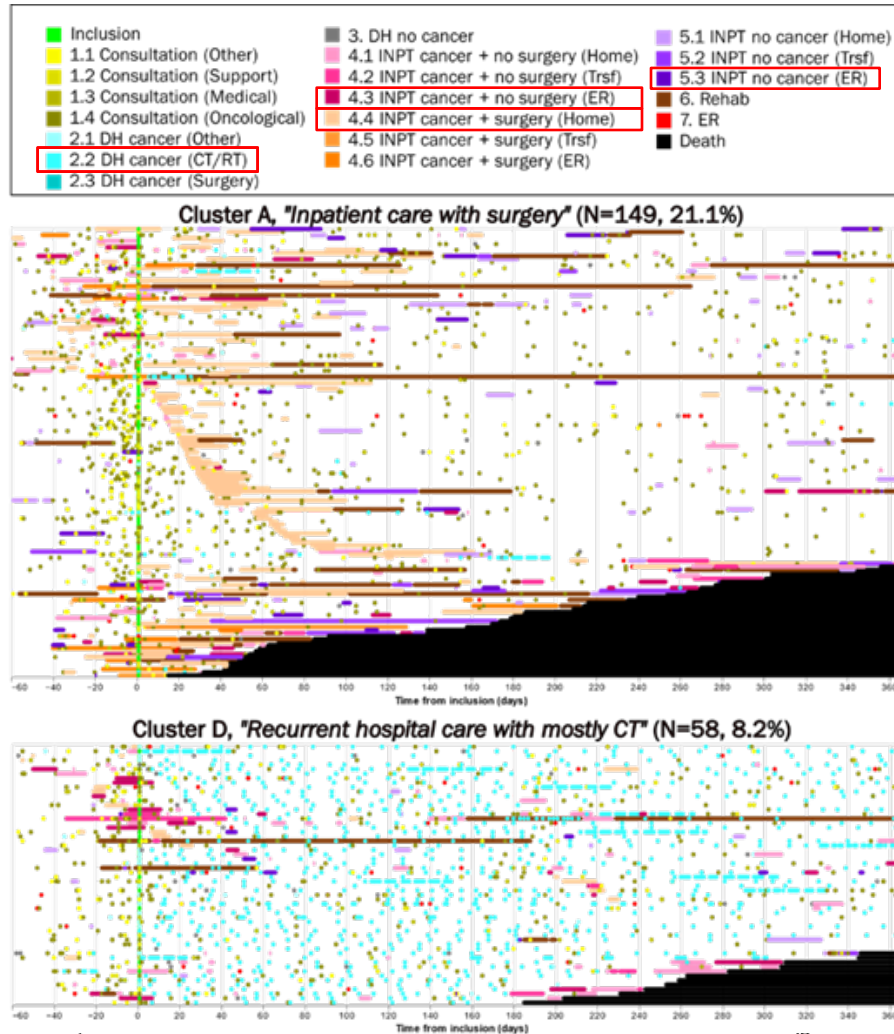
Monitoring and management

Innovation

Source: Doutreligne M, et al. Good practices for clinical data warehouse implementation: A case study in France. PLOS Digit Health. 2023 Jul 6;2(7):e0000298. doi: 10.1371/journal.pdig.0000298.

# Real-life trajectories modelling

## Identify patterns of healthcare use

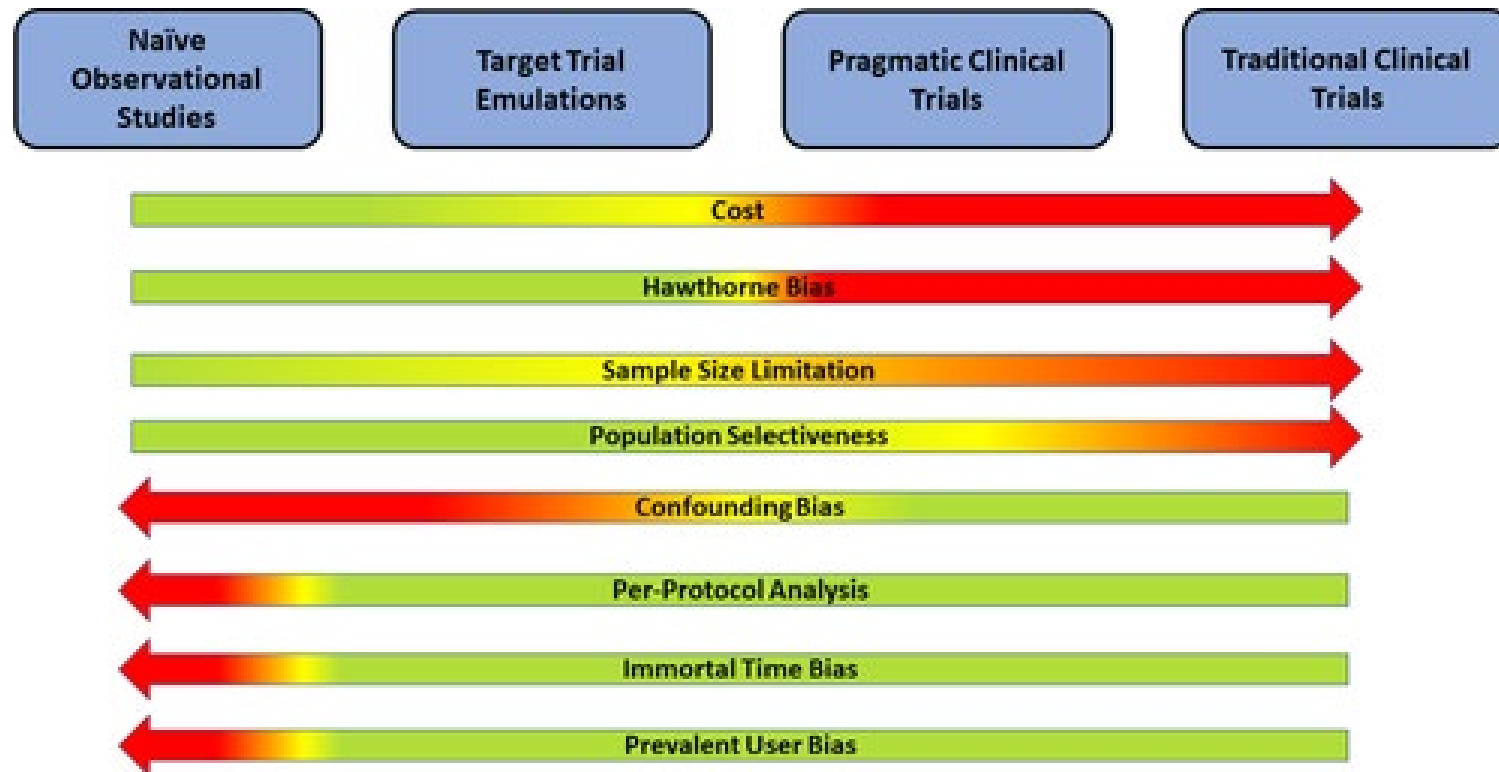


Source: JEAN C, et al. Hospital Care Trajectories of Older Adults with Cancer and the Associated Clinical Profiles: linking a French Prospective Cohort Study and a Clinical Data Warehouse. (SIOG 2023 & Submitted)

# Predicting treatment effectiveness and survival

## Emulated target trials

Emulated target trials are used for comparative effectiveness research on observational data, when RCTs are unavailable. (Hernan and Robins., *Am J Epidemiol.*, 2016;183(8):758–764)



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Nécessite une expertise pour l'analyse et l'interprétation (prise en compte des biais)

# REAL WORLD DATA

