

Efficient Patient Recruitment for
Innovative Clinical Trials of
Existing Drugs to other Indications

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 eHealth



PONTE: A Context-Aware Approach for Automated Clinical Trial Protocol Design

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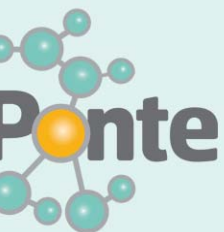


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Layout

- Introduction to the PONTE EU project
- A Context-Aware Architecture for CTP design
 - Architecture
 - Context-Aware Parameters
- Decision Support
- Intelligent Semantic Search
- Real-World Scenario: An example of usage



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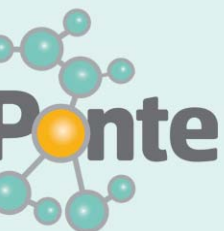
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Introduction to the PONTE EU Project

- Average Drug Development **cost** : €500-700 million per drug candidate - **timeline** : more than 10 years.
- Tremendous reduction in **new active ingredients** reaching the market yearly:
 - ~ 60/year (late 1980s), 52 (1991), 31 (2001), 20-25 (currently)
- Clinical trials :
 - ~ 1/3 of the costs of drug development half of which depends on duration
 - Low recruitment rates – Long recruitment periods
 - Subjects recruited represent only partially the target patient population
 - Mortality rates in clinical study findings vs real life
 - 1 out of 5000 new drug candidates reach the market
- *Drug repositioning trend* and *Complex tests of hypothesis*: testing new treatments of existing drugs on patients suffering from another disorder
- Humans' high variability in response to a drug treatment requires *large-scale clinical trial conduction* for ensuring that the investigational treatment is safe and effective



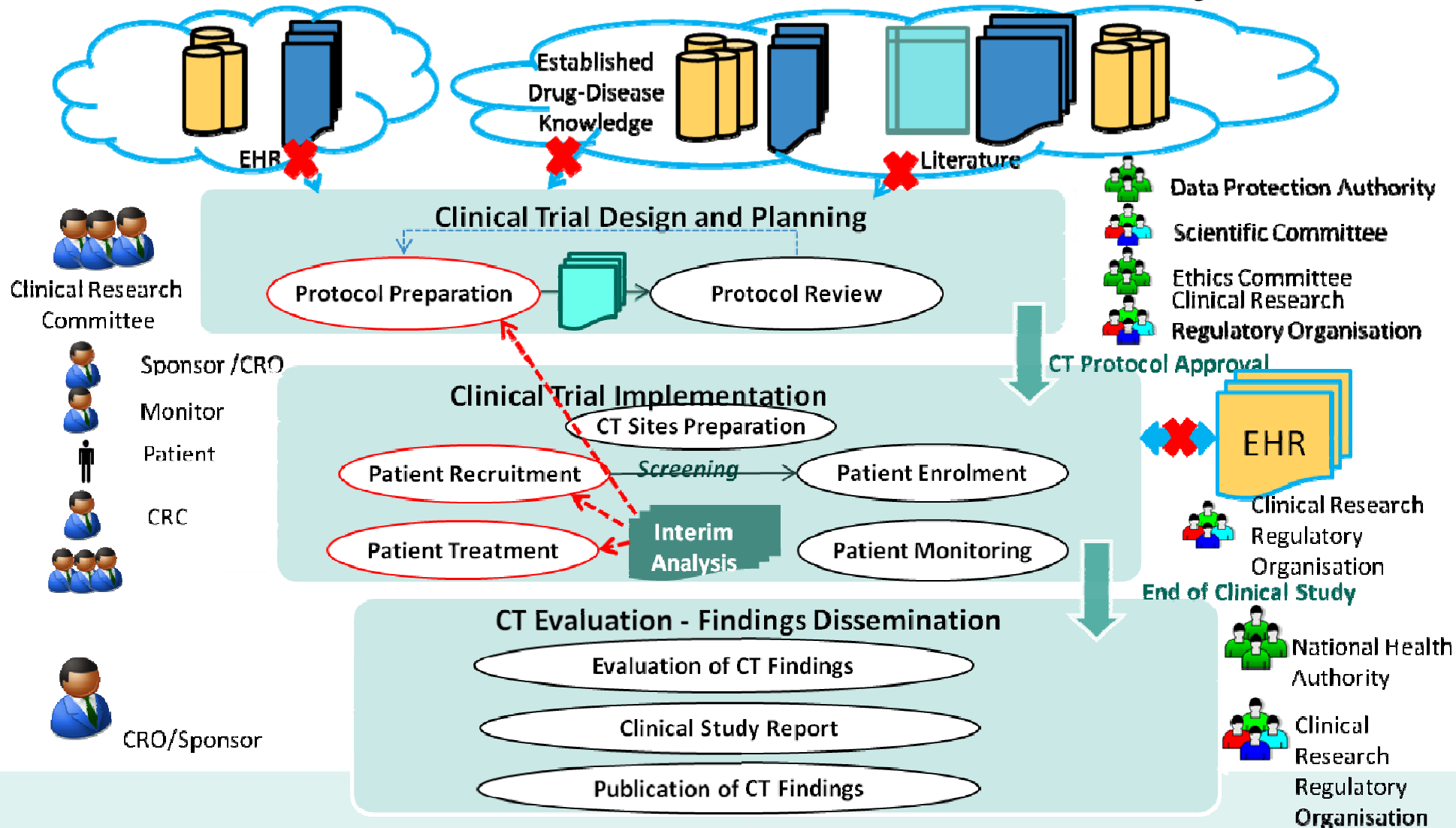
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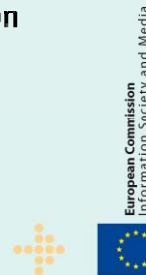


Clinical Trials: Currently



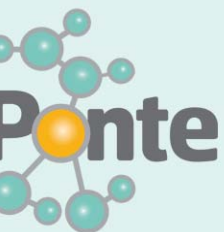
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The PONTE Solution

- Development of a research question into a Clinical Trial
- Clinical Trial design management
 - Effective decision support
 - Efficient navigation capabilities
 - Adaptive Study Design
 - Intelligent semantic search in distributed drug, disease and clinical trials data sources
- Secure and Privacy-preserving interlinking with EHRs



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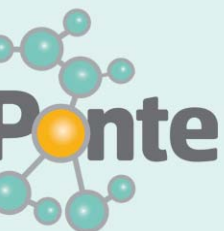
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The PONTE platform

- Test of Hypothesis Evaluation
- Clinical Trial Protocol Authoring Tool
- Intelligent search of data sources through the platform (PubMed, ClinicalTrials.org, drug/disease data)
- Guidance in the determination of study parameters through available predefined queries and efficient decision support services
- Adaptive clinical trial design by evaluating the level of confidence for each protocol parameter
- Efficient determination of target population focusing on patient safety, clinical trial efficacy and cost



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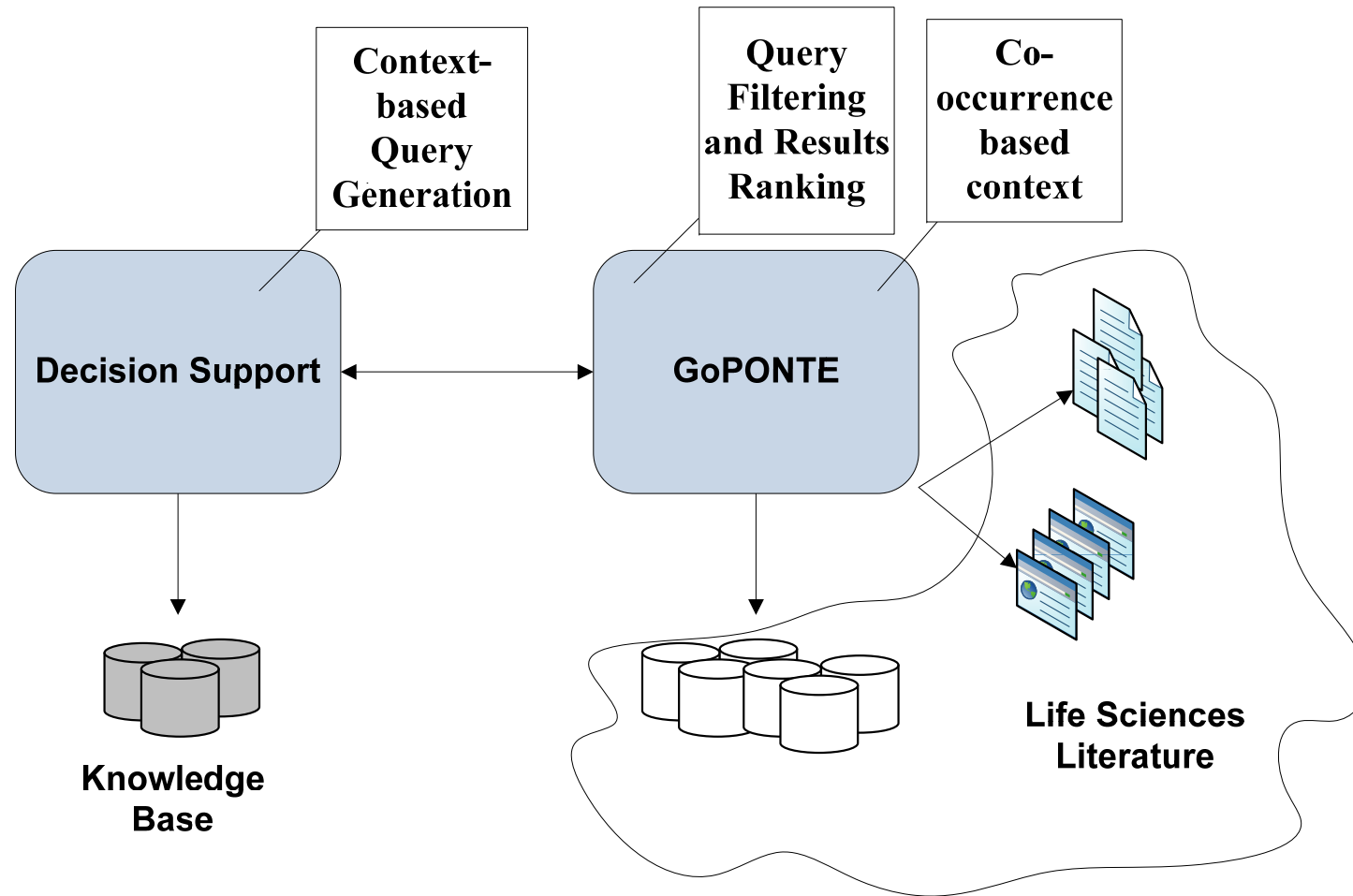
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A Context-Aware Architecture for CTP Design



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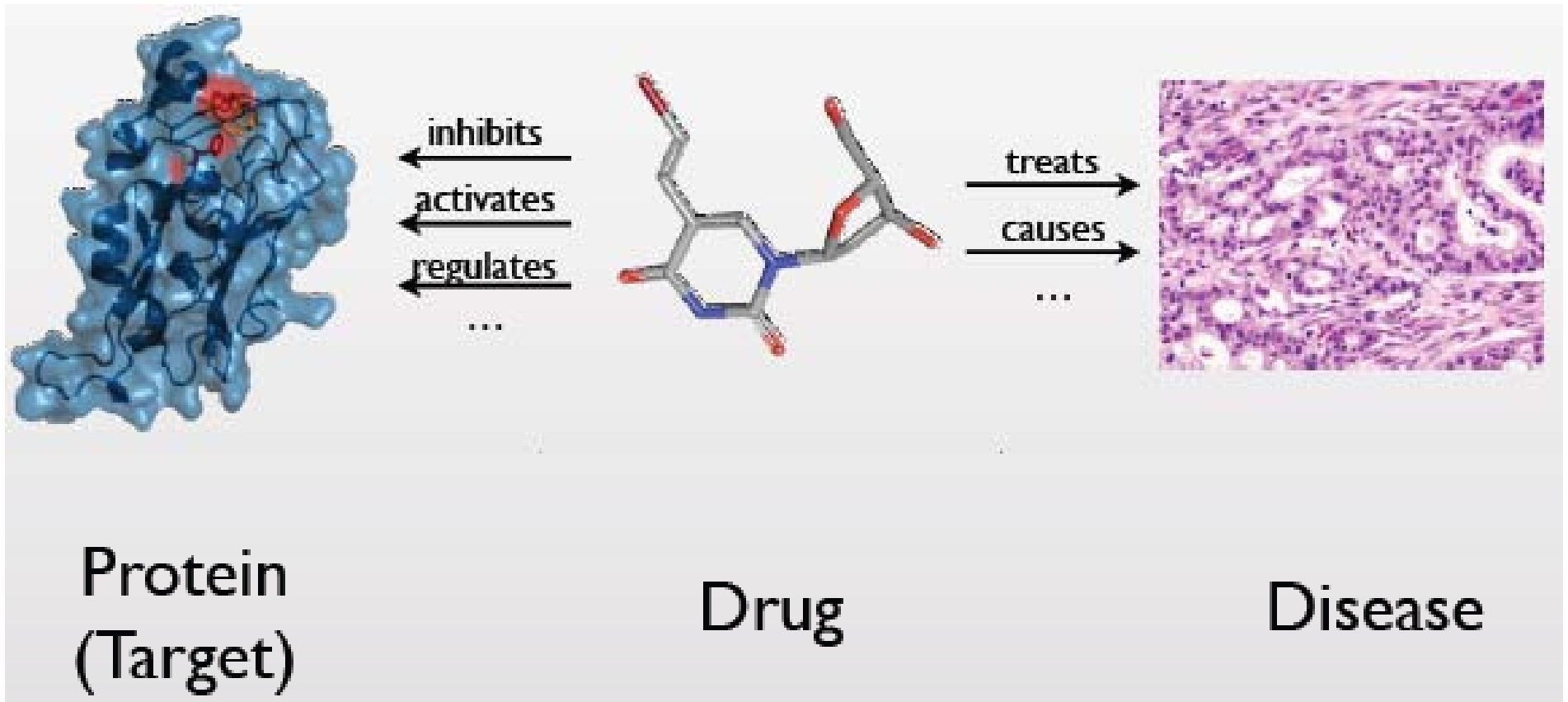
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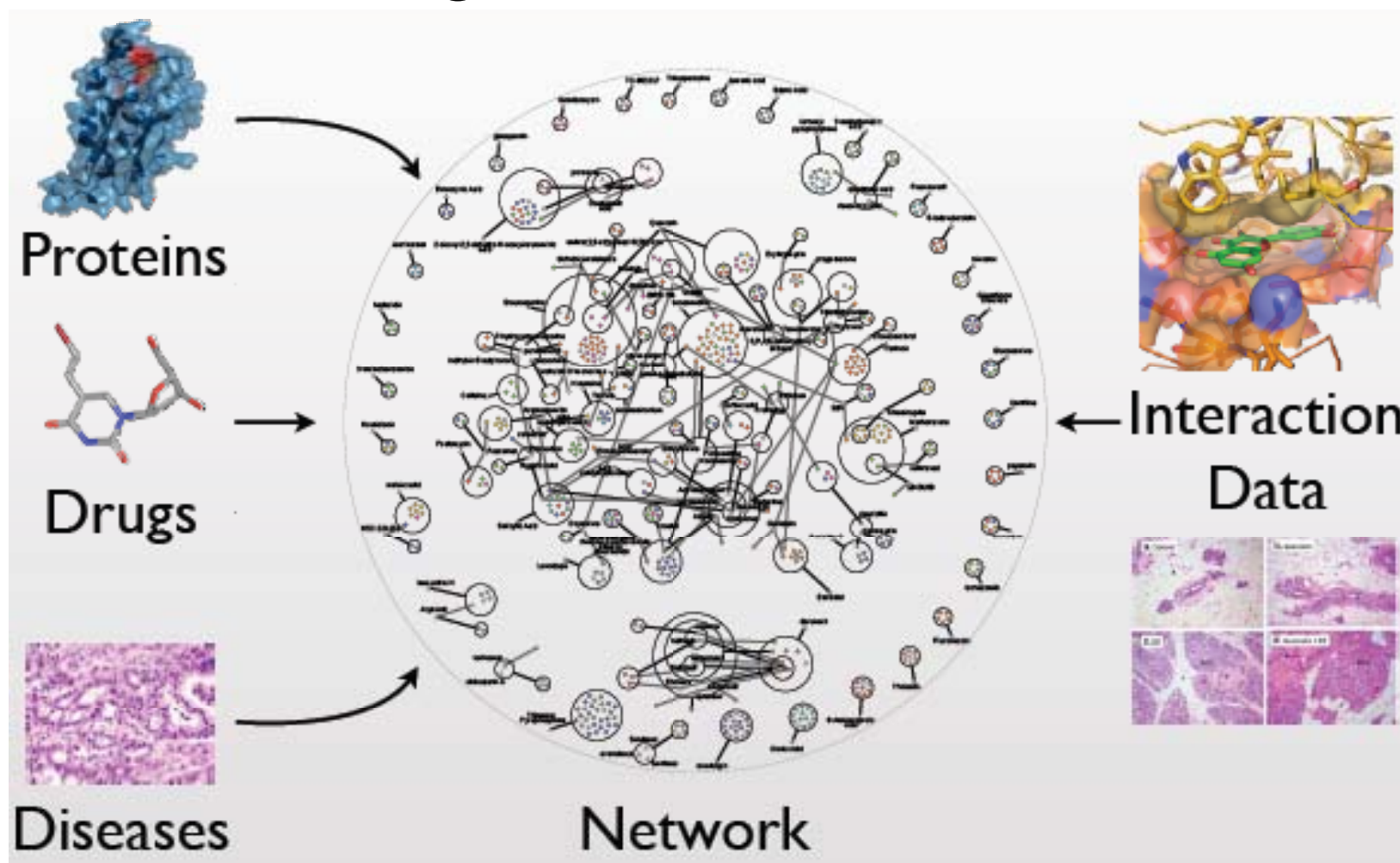
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Context-Aware Parameters



The Power of Biological Networks and Linked-Data



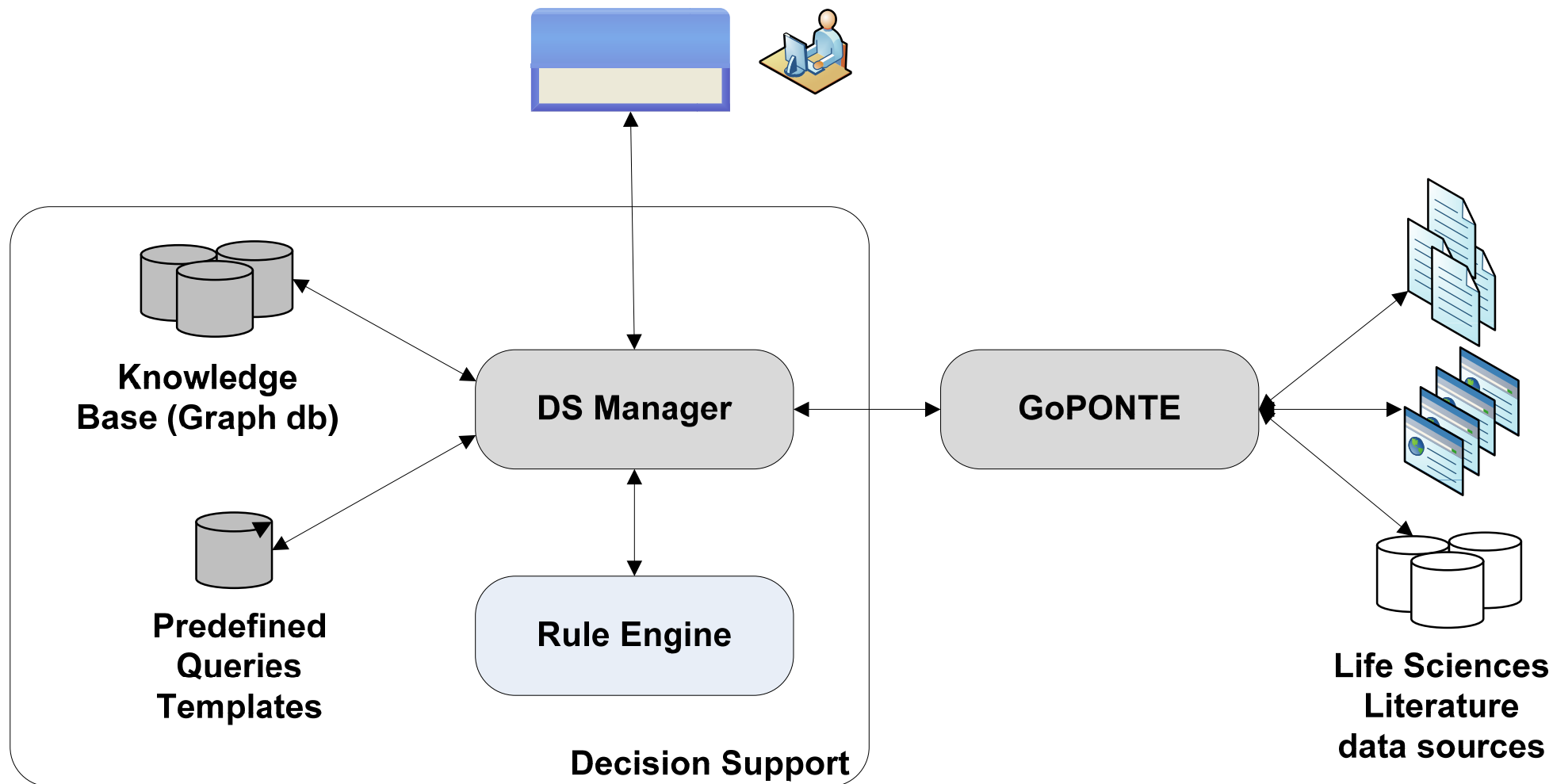
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Context-Aware Decision Support



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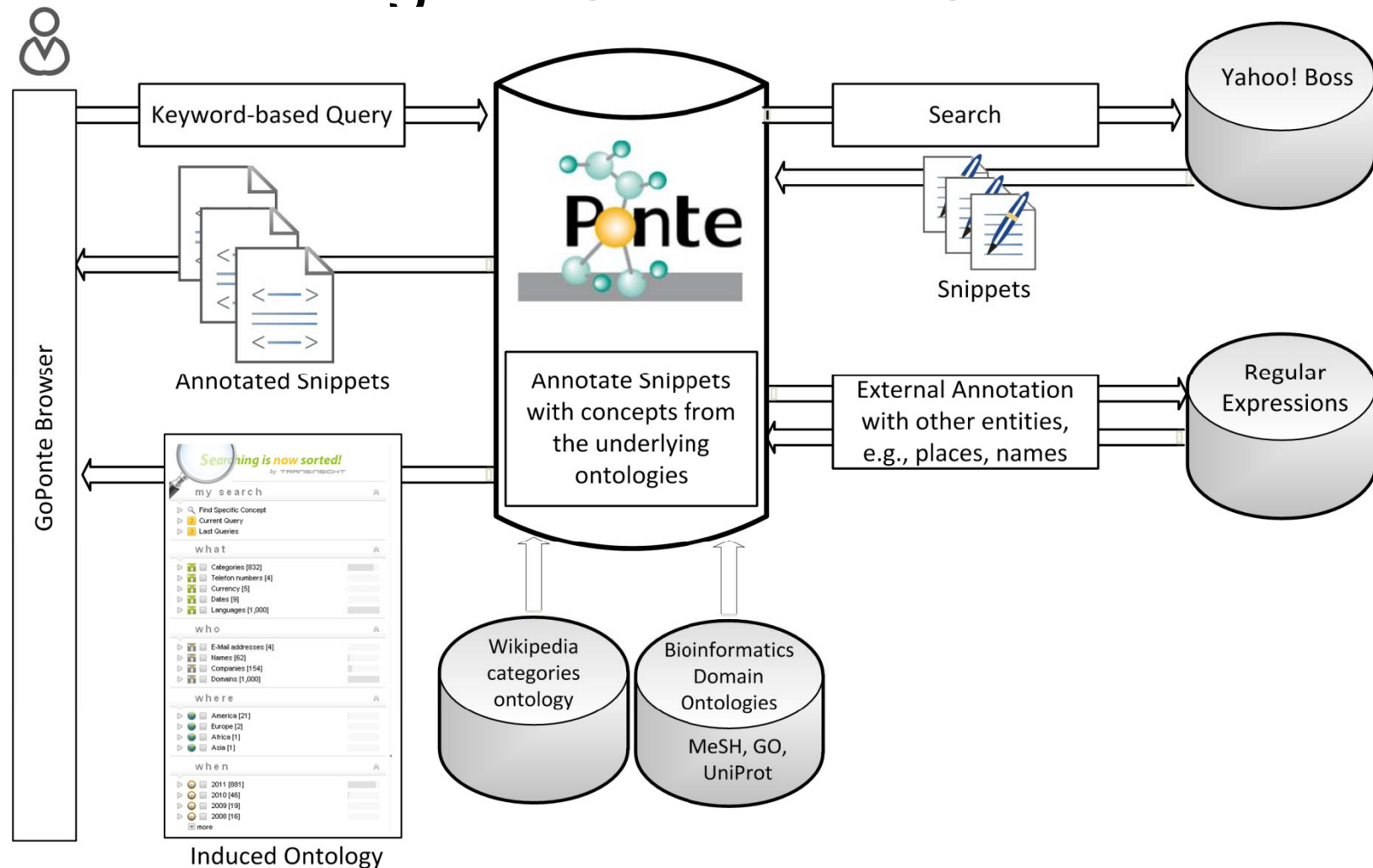
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Intelligent Semantic Search



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Real-World Scenario: Example of Usage

- Drug: Amiodarone
- Disease: acute myocardial infarction
- Targets: May be retrieved automatically from DS and GoPonte
- Automatically generated queries:

Predefined Queries

Epidemiology of the Acute myocardial infarction
Acute myocardial infarction pathophysiology
Standard Treatments for Acute myocardial infarction
Comorbidities of the Acute myocardial infarction

amiodarone interactions with other drugs
amiodarone interactions with food
amiodarone AND potassium voltage-gated channel, subfamily H (eag-related), member 2(KCNH2)
amiodarone AND adrenergic, beta-1-, receptor(ADRB1)
amiodarone AND adrenergic, alpha-1A-, receptor(ADRA1A)
amiodarone AND adrenergic, alpha-1B-, receptor(ADRA1B)
amiodarone AND adrenergic, alpha-1D-, receptor(ADRA1D)
amiodarone AND cytochrome P450, family 2, subfamily D, polypeptide 6(CYP2D6)
amiodarone AND cytochrome P450, family 2, subfamily C, polypeptide 9(CYP2C9)
amiodarone AND cytochrome P450, family 1, subfamily A, polypeptide 2(CYP1A2)
amiodarone AND cytochrome P450, family 3, subfamily A, polypeptide 4(CYP3A4)
amiodarone AND Resting heart rate, 607276
amiodarone AND Long QT syndrome-2



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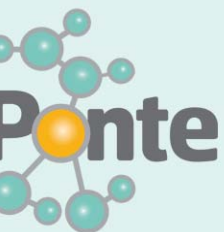
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Context-Aware and Automatically Guided Semantic Search

The screenshot displays a web-based semantic search interface. On the left, a sidebar contains a hierarchical list of categories under the heading "what". The "Risk Factors" category is highlighted with a red box. The main search area shows a search bar with the query "myocardial infarction epidemiology site:www.ncbi.nlm.nih.gov \"Risk Factors\"[mesh]" and a "find it" button. Below the search bar, a notification states "164 of 5,370 documents semantically analyzed". The search results are displayed under the heading "documents" and include three entries:

- 7: Risk factors for non-fatal myocardial infarction in young South ...** [2012-05-13]
1 Clinical **Epidemiology** Unit, Department of **Community Health Sciences**, Aga Khan University, Karachi, Pakistan
www.ncbi.nlm.nih.gov/pmc/articles/PMC1768096
Wikipedia: Communities, Community, Domicile, Epidemiology, Infarction, Myocardial Infarction, Myocardial infarct, Myocardial infarctions, Neighborhood, Place of birth, Risk factor, ScienCe
- 18: Circulating influenza virus, climatic factors, and acute ...** [2012-05-16]
Myocardial Infarction/epidemiology* **Myocardial Infarction/mortality**, **Poisson Distribution**, **Risk Factors**; **Sentinel Surveillance**; Wales/**epidemiology**; Grant Support
www.ncbi.nlm.nih.gov/pubmed/21606529
Wikipedia: Age-specific death rate, Animal virus, Case fatality rate, Death Rate, Death rates, Distribution, Epidemiology, Grippe, Human flu, Human influenza, Infarction, Influenza, Influenza, human, Influenza Virus, Mortality, Myocardial Infarction, Myocardial infarct, Myocardial infarctions, Orthomyxoviridae, Orthomyxovirus, Poisson Distribution, Risk factor, Virus
- 23: Major habitual dietary patterns are associated with acute ...** [2012-05-10]
Myocardial Infarction/blood; **Myocardial Infarction/epidemiology*** **Odds Ratio**, Portugal/**epidemiology**; **Questionnaires**; **Risk Factors**; **Sex Factors**; **Vegetables**; Substances
www.ncbi.nlm.nih.gov/pubmed/21272698
Wikipedia: Epidemiology, Infarction, Myocardial Infarction, Myocardial infarct, Myocardial infarctions, Odds ratio, Patterns, Questionnaire, Risk factor, Risk ratio, Sex factor, Vegetable



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Thank You

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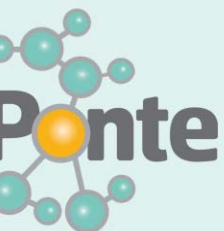


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2nd iteration:: Dissemination

System	Document Type	Ontologies	Text Mining	Results type
	Web pages/documents	-	synonym expansion	snippets
	Abstracts, xml	Gene Ontology, MeSH	entities and concepts recognition, annotation (classification)	Snippets, induced ontology, abstracts
	Abstracts	Gene Ontology, MeSH , PONTE	entities and concepts recognition, annotation (classification)	Snippets, induced ontology
	Abstracts, semi-structured documents, web pages	PONTE	entities and concepts recognition, annotation (classification)	Snippets, induced ontology, abstracts/documents



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Discussion of Functionality: Linked Data



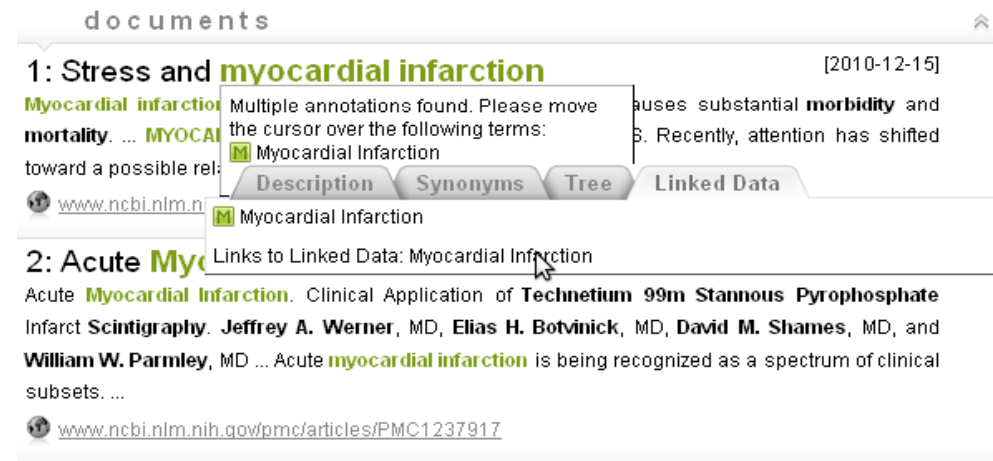
documents

1: Stress and **myocardial infarction** [2010-12-15]

Myocardial infarction (MI) is a serious health problem which causes substantial **morbidity** and **mortality**. ... **MYOCARDIAL INFARCTION** AND SPORTING EVENTS. Recently, attention has shifted toward a possible relation between cardiovascular ...

www.ncbi.nlm.nih.gov/pmc/articles/PMC1767636

Single search results with search terms highlighted in green further identified entities in bold, hyperlink to full text in grey (bottom), and export button (upper left).



documents

1: Stress and **myocardial infarction** [2010-12-15]

Myocardial infarction mortality. ... **MYOCARDIAL INFARCTION** toward a possible relation between cardiovascular ...

www.ncbi.nlm.nih.gov/pmc/articles/PMC1767636

2: Acute **Myocardial Infarction**. Clinical Application of **Technetium 99m Stannous Pyrophosphate** Infarct **Scintigraphy**. **Jeffrey A. Werner**, MD, **Elias H. Botvinick**, MD, **David M. Shames**, MD, and **William W. Parmley**, MD ... Acute **myocardial infarction** is being recognized as a spectrum of clinical subsets. ...

www.ncbi.nlm.nih.gov/pmc/articles/PMC1237917

Multiple annotations found. Please move the cursor over the following terms:

- Myocardial Infarction
- Myocardial Infarction

Description Synonyms Tree Linked Data

Links to Linked Data: Myocardial Infarction

Starting the expansion of the search to the Linked Data for the term “myocardial infarction” by clicking on the corresponding entry.



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