**Patient Scenario with Data Sourcing –Industry & Trial Component Associated**

* 1. Patient [patient role OBI:0000093] (and family members [NCI: Patient\_Family\_Member\_or\_Friend CL357040]) report symptoms [IDO:0000048 Symptom] to ~~physician~~ clinician [NCI Thesaurus: Physician]
* 2. Physician [NCI Thesaurus: Physician] makes initial working diagnosis [OBI:0000075] of Disease [DOID: 10652] or “List of Differential Diagnoses” (For the purpose of this use case – Alzheimer’s Disease will be the primary focus)
* 3. Physician arranges for patient to have a basic biochemical/haematological, and SNP profile undertaken. Biochemistry and Haematology requests are input by respective departments directly into patient’s eRecord from laboratory. SNP and genetic data will be submitted directly to the NIH Pharmacogenetics Research Network (PGRN). The main purposes will be to obtain the following information as this specific data source strives to provide :

 “The work of the various groups listed ranges from basic research into identifying variation in genes (and functional consequences) relevant to pharmacogenetics, to clinical research aimed at understanding the **genetic basis for variable drug responses, both therapeutic and adverse.” -** see more detail below

To Note : A list of “intended medications for use” will be supplied to this data source as they become identified in the following several steps to aid and supplement the SNP data sent at this early stage. The ultimate purpose : To enable PGRN to facilitate goals to “personalize” the proposed therapy(ies).

**The Ontology will source (Free at present):**

**1.The NIH Pharmacogenetics Research Network (PGRN)**

<http://www.pharmgkb.org/>

**{Background Taken from Website for brief overview of functions}**

**Mission**

**The mission of the NIH PGRN is to advance our knowledge of the genetic basis for variable drug responses.**

**Background**

The NIH Pharmacogenetics Research Network (PGRN) was formed in 2000 to enable a network of multi-disciplinary research groups to conduct studies addressing research questions in pharmacogenetics and pharmacogenomics (the genetic basis for variation in drug responses) and to populate a knowledge base (PharmGKB). The latter will be used as a research tool to enable future pharmacogenetics studies and should serve as the premier knowledge base in the field. In 2005, the PGRN was renewed for a second 5-year period. The PGRN has been led by NIGMS, with important participation from other NIH Institutes and Offices, including NHLBI, NIDA, NCI, NIEHS, NHGRI, NIMH, NLM and ORWH. Ultimately, the long term goal is to translate this knowledge and identify safe and effective drug therapies designed for individual patients.

**Organization**

The PGRN comprises 12 independently-funded interactive research groups, including the knowledge base group. Each research group has a focus in an identified area of pharmacogenetics (see [members page](http://www.pharmgkb.org/network/pharmacogenetics_research_network.jsp) for a full description of the PGRN research groups and their specific interests). The PGRN is accomplishing its mission by conducting studies of variation in human genes relevant to pharmacokinetics (drug disposition) and pharmacodynamics (drug action), and the relationship of such variation to drug response phenotypes, with deposition of the resulting data into the knowledge base, [PharmGKB](http://www.pharmgkb.org). PharmGKB contains both raw and curated information. It presents data and information accumulated in the field and contributed by researchers both within and beyond the network.

**Goals**

All PGRN groups are expected to advance pharmacogenetics research knowledge in their respective areas of focus. The work of the groups ranges from basic research into identifying variation in genes (and functional consequences) relevant to pharmacogenetics, to clinical research aimed at understanding the **genetic basis for variable drug responses, both therapeutic and adverse.** The aims of the PGRN include:

* **Performing the highest quality research studies** to understand and explain the relationships between drug response phenotypes and genetic variation, using state-of-the-art experimental approaches and technologies.
* **Building a premier web-based knowledge base (PharmGKB)** that rapidly disseminates accurate and detailed definitions of genotypes and phenotypes in pharmacogenetics,
along with tools and resources.
* **Stimulating collaborations within and beyond the PGRN** through having a critical mass of researchers in cross-cutting areas.
* **Interacting with and influencing the wider community of scientists** in academia, industry, and government regulatory agencies, to advance the field.
* 4. A follow up meeting is scheduled by the clinician to perform a set of diagnostic tests outlined by what the clinician feels initially are most appropriate for disease presentation.
* 5. Physician goes to ‘interface’(at any point) and continues to add investigations/lab results and these are combined with the patient’s medical history (occupational exposure, concurrent medication, lifestyle information), and a disease (AD ) is chosen as the most likely of the listed differential diagnoses based on all of the information provided. (This is real time information).

The ontology consults data sources that are linked to supply the user with suggested diagnostic criteria for given differential diagnosis (Example – Alzheimer’s Disease AD will be used throughout) :

**Free Sources** :

The [**National Institute of Neurological and Communicative Disorders and Stroke**](http://en.wikipedia.org/wiki/National_Institute_of_Neurological_and_Communicative_Disorders_and_Stroke), and the [**Alzheimer's Disease and Related Disorders Association**](http://en.wikipedia.org/wiki/Alzheimer%27s_Disease_and_Related_Disorders_Association) (now known as the Alzheimer's Association) and are among the most used in the diagnosis of [Alzheimer's disease](http://en.wikipedia.org/wiki/Alzheimer%27s_disease) (AD).

The **Diagnostic and Statistical Manual of Mental Disorders** [DSM-IV-TR](http://en.wikipedia.org/wiki/DSM-IV-TR%22%20%5Co%20%22DSM-IV-TR) criteria published by the [American Psychiatric Association](http://en.wikipedia.org/wiki/American_Psychiatric_Association) (DSM) also provides specialist diagnostic criteria for [mental disorders](http://en.wikipedia.org/wiki/Mental_disorder). This includes Alzheimer’s Disease.

**Sample Clinical Sources at a fee to user and limited by institution using ontology :**

|  |
| --- |
| Harrison's Online <http://www.accessmedicine.com/resourceTOC.aspx?resourceID=4>Featuring the complete contents of *Harrison's Principles ofInternal Medicine, 17e* Anthony S. Fauci, Eugene Braunwald, Dennis L. Kasper, Stephen L. Hauser, Dan L. Longo, J. Larry Jameson, and Joseph Loscalzo, Eds |

**Oxford Textbook of Medicine**Fifth Edition Edited by David A. Warrell, Timothy M. Cox and John D. Firth ISBN13: 9780199204854ISBN10: 0199204853 Hardback, 4500 pages Mar 2010,  Not Yet Published

* 6. ‘Interface’ provides clinician, via these data sources, with further diagnostic tests for AD that should be performed based not only on diagnostic criteria, but on available clinical practice guidelines :

**The Ontology will source national guidelines (Free source at present):**

**1.The National Institute for Health and Clinical Excellence (NICE)** is the independent organisation responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health.
Read more about [who we are](http://www.nice.org.uk/aboutnice/whoweare/who_we_are.jsp).

## What we do

NICE produces guidance in three areas of health:

* public health - guidance on the promotion of good health and the prevention of ill health for those working in the NHS, local authorities and the wider public and voluntary sector
* health technologies - guidance on the use of new and existing medicines, treatments and procedures within the NHS
* clinical practice - guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS.

The booklet [NICE: our guidance sets the standard for good healthcare](http://www.nice.org.uk/aboutnice/?domedia=1&mid=EE5AA72F-19B9-E0B5-D4215C860E77FD2E) explains more about NICE and the types of guidance we produce.

Read more about [what we do](http://www.nice.org.uk/aboutnice/whatwedo/what_we_do.jsp).

## How we work

NICE guidance is developed using the expertise of the NHS and the wider healthcare community including NHS staff, healthcare professionals, patients and carers, industry and the academic world.

**2. The National Guideline Clearinghouse™ (NGC)**

**guideline.gov**

**About NGC**

The National Guideline Clearinghouse™ (NGC) is a comprehensive database of evidence-based clinical practice guidelines and related documents. NGC is an initiative of the [Agency for Healthcare Research and Quality (AHRQ)](http://www.ahrq.gov), U.S. Department of Health and Human Services. NGC was originally created by AHRQ in partnership with the [American Medical Association](http://www.ama-assn.org) and the [American Association of Health Plans](http://www.aahp.org/template.cfm) (now America's Health Insurance Plans [AHIP]).

The [NGC mission](http://www.guideline.gov/about/mission.aspx) is to provide physicians, nurses, and other health professionals, health care providers, health plans, integrated delivery systems, purchasers and others an accessible mechanism for obtaining objective, detailed information on clinical practice guidelines and to further their dissemination, implementation and use.

### Key components of NGC include:

* Structured abstracts (summaries) about the guideline and its development
* Links to full-text guidelines, where available, and/or ordering information for print copies
* Palm-based [PDA Downloads](http://www.guideline.gov/about/pdadownload.aspx) of the Complete NGC Summary for all guidelines represented in the database.
* A [Guideline Comparison](http://www.guideline.gov/about/GuidelineComparisonDescrip.aspx) utility that gives users the ability to generate side-by-side comparisons for any combination of two or more guidelines
* Unique guideline comparisons called [Guideline Syntheses](http://www.guideline.gov/about/synthesis.aspx) prepared by NGC staff, compare guidelines covering similar topics, highlighting areas of similarity and difference. NGC Guideline Syntheses often provide a comparison of guidelines developed in different countries, providing insight into commonalities and differences in international health practices.
* An electronic forum, [NGC-L](http://www.guideline.gov/resources/discussion_list.aspx) for exchanging information on clinical practice guidelines, their development, implementation and use
* An [Annotated Bibliography](http://www.guideline.gov/ab/default.aspx) database where users can search for citations for publications and resources about guidelines, including guideline development and methodology, structure, evaluation, and implementation
* An [Expert Commentary](http://www.guideline.gov/resources/expert_commentary.aspx) feature written/reviewed by the NGC/NQMC [Editorial Board](http://www.guideline.gov/about/editorial_board.aspx)

### Other user-friendly features include the following:

* [What's New](http://www.guideline.gov/whatsnew/whatsnew.aspx) enables users to see what guidelines have been added each week and includes an index of all guidelines in NGC.
* [NGC Update Service](http://www.guideline.gov/whatsnew/register.aspx) is a weekly electronic mailing of new and updated guidelines posted to the NGC Web site.
* [Detailed Search](http://www.guideline.gov/search/detailedsearch.aspx) enables users to create very specific search queries based on the various attributes found in the [NGC Classification Scheme](http://www.guideline.gov/about/classification.aspx).
* [NGC Browse](http://www.guideline.gov/browse/browse.aspx) permits users to scan for guidelines available on the NGC site by disease/condition, treatment/intervention, or developing organization.
* [PDA/Palm List](http://www.guideline.gov/resources/pda.aspx) provides users with information regarding the availability of full-text guidelines and/or companion documents available through the guideline developer, that can be downloaded for the handheld computer (Personal Digital Assistant [PDA], Palm, etc.)
* The [AHRQ Evidence Reports](http://www.guideline.gov/resources/ahrq_products.aspx) page provides a list and links to various reports produced under AHRQ's Evidence-based Practice Program and Effective Health Care Program.
* [Glossary](http://www.guideline.gov/resources/glossary.aspx) provides definitions of terms used in the standardized abstracts (summaries).
* 7. Physician confirms and now has a refined and widely acceptable diagnosis of AD with behavioural assessments, cognitive tests, and appropriate brain scan if indicated and enters data into the patient’s eHR

**The Ontology will source :**

<http://www.who.int/classifications/icd/en/>

**International Classification of Diseases (ICD)**

ICD-10 was endorsed by the Forty-third World Health Assembly in May 1990 and came into use in WHO Member States as from 1994. The classification is the latest in a series which has its origins in the 1850s. The first edition, known as the International List of Causes of Death, was adopted by the International Statistical Institute in 1893. WHO took over the responsibility for the ICD at its creation in 1948 when the Sixth Revision, which included causes of morbidity for the first time, was published. The World Health Assembly adopted in 1967 the WHO Nomenclature Regulations that stipulate use of ICD in its most current revision for mortality and morbidity statistics by all Member States.

The ICD is the international standard diagnostic classification for all general epidemiological, many health management purposes and clinical use. These include the analysis of the general health situation of population groups and monitoring of the incidence and prevalence of diseases and other health problems in relation to other variables such as the characteristics and circumstances of the individuals affected, reimbursement, resource allocation, quality and guidelines.

It is used to classify diseases and other health problems recorded on many types of health and vital records including death certificates and health records. In addition to enabling the storage and retrieval of diagnostic information for clinical, epidemiological and quality purposes, these records also provide the basis for the compilation of national mortality and morbidity statistics by WHO Member States.

* 8. Physician goes to the ‘interface’ to select the most appropriate AD drug & clinical protocol based on the severity of the disease, patient’s SNP profile (ADME, efficacy/safety (based on presence or absence of receptors)), patient’s BMI, and availability on Medicare D

**Five fundamental questions will be answered by the ontology at this stage by sourcing the following five data sets simultaneously or in a particular order.**

* 1. What are the recommended agents by clinical guidelines pr practice guidelines
	2. What products are available to prescribe, and which are legally indicated for disease AD?
	3. What is the SNP verdict? These agents are sourced with pharmacogenomics database **Pharmacogenetics Research Network (PGRN)** to determine
		+ Will they be efficacious? Receptor positive disease?
		+ Will they be harmful? Toxic metabolites? Available CYP 450 or acetylator status?
	4. Are the resulting agents covered by the patient’s specific insurance? (In real time)

Are the preceding predictive genetic SNP tests covered by the patient’s insurance company? They may be recommended and indicated **prior** to treatment as in HIV medication ABACAVIR.

A.Guidelines and literature sources above list pharmaceutical agents that are indicated for use in condition (AD)

B. What are the available licensed products we can choose to prescribe? Are these agents legally indicated for AD? Are they even available?

pdr.net

**PDR.net** is a web portal where healthcare professionals can access specialty-focused clinical resources, including drug and disease information, patient education, specialty news, journal abstracts, conference information, and more.

**Registered PDR.net users have access to**:

* Full FDA-approved product labeling
* Multi-drug interaction checker
* Daily news updates
* PDR eBooks
* Opportunities for receiving drug samples
* eDetail opportunities
* PDR's concise drug information
* Specialty-focused resource centers
* Drug alerts and news
* MEDLINE & Stedman's Medical Dictionary
* Patient education
* Our point-of-care PDA download for clinical decision support
* Professional resources such as a FREE download of Evidence Xpert, an evidence-based application for your PDA device

C.The NIH Pharmacogenetics Research Network (PGRN)

<http://www.pharmgkb.org/>

D. Examples of insurers :

**Medicare Formulary Finder for Prescription Drug Plans** Top of Form



Bottom of Form

|  |
| --- |
|   |
| Welcome to the Formulary Finder for Prescription Drug Plans. This tool will allow you to find plans in your state that match your required drug list. |  |  |

 <http://formularyfinder.medicare.gov/formularyfinder/selectstate.asp?javascripton=true>

**The Blue Cross and Blue Shield Association (BCBSA)** is a national federation of 39 independent, community-based and locally operated Blue Cross and Blue Shield companies.

Throughout our 80-year history, the 39 [Blue Cross and Blue Shield companies](http://www.bcbs.com/coverage/find/plan/) have provided millions of families with top-quality, affordable health insurance.

<http://www.bcbs.com/>

8b.The physician checks with pharmacist, or consults drug information literature to avoid potential drug interactions :

**Ontology sources** :

**FACTS & COMPARISONS®**

For more than sixty years, Facts & Comparisons®, a part of Wolters Kluwer Health, has been the pharmacists’ source for drug information. Via print, CD-ROM, PDA or Internet, Facts & Comparisons® offers trusted, unbiased drug information.
For more information, visit [FactsandComparisons.com](http://www.factsandcomparisons.com) or call 800.223.0554.

* **9. Physician now prescribes Aricept (Donepezil) as it satisfies criteria A through D above**
* **It is indicated, safe, effective, available, there are no drug interactions issues with drug delivery, and most importantly, it is covered.**
* 10. In follow up, patient later reports nausea from donepezil, and physician is aware of this common side effect (other side effects reported include bradycardia, diarrhea, anorexia, abdominal pain, and vivid dreams etc…) re-consults literature to insure this is acceptable and agreeable with patient. If not, revisit loop above. Document side effect for post marketing adverse event pick up, and future study. Change medication if necessary or add another medication to alleviate side effects.

**The ontology sources the following to enable clinician to reassure patient :**

**{2 well respected drug information source} – at a fee ( to contact for trial access)**

<http://www.micromedex.com/>

Thomson Reuters is the leading provider of decision support solutions that help organizations across the healthcare industry improve clinical and business performance. It is built on the strength of leading healthcare brands including Medstat, MercuryMD, Micromedex, PDR, and Solucient. Through these offerings, Thomson Reuters provides the solutions, information, insight, and analysis its healthcare customers need to manage healthcare cost, quality, market positioning, and enterprise growth.

* Our solutions are comprised of comprehensive healthcare databases, analytics, professional services, and research services to help professionals make better decisions faster. Thomson Reuters offers healthcare business solutions for clinicians, hospitals and healthcare providers, employers, health plans, government agencies, pharmaceutical companies and researchers.
* Organizations across the healthcare industry rely on Thomson Reuters to diagnose and treat patients anywhere at anytime; improve clinical, financial, and operational performance; and develop sound growth plans and effective marketing strategies. Thomson Reuters also assists its healthcare customers in designing effective benefits plans, targeting and evaluating preventative medicine programs, structuring disease management programs, improving access to care, and stewarding government dollars.
* Through its legacy brands, Thomson Reuters has been a trusted partner to healthcare decision makers, delivering reliable and innovative solutions since 1944 - longer than any other company in the industry. Professionals and stakeholders from every facet of healthcare use Thomson Reuters solutions to understand markets, access medical and drug information, manage costs, and improve the quality of healthcare. For more information, go to [www.thomsonreuters.com/healthcare](http://www.thomsonreuters.com/healthcare).
* Thomson Reuters is the world's leading source of intelligent information for businesses and professionals. We combine industry expertise with innovative technology to deliver critical information to leading decision makers in the financial, legal, tax and accounting, scientific, healthcare and media markets, powered by the world’s most trusted news organization. With headquarters in New York and major operations in London and Eagan, Minnesota, Thomson Reuters employs more than 50,000 people in 93 countries. Thomson Reuters shares are listed on the New York Stock Exchange (NYSE: TRI); Toronto Stock Exchange (TSX: TRI); London Stock Exchange (LSE: TRIL); and Nasdaq (NASDAQ: TRIN). For more information, go to [www.thomsonreuters.com](http://www.thomsonreuters.com)

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For more information, visit [FactsandComparisons.com](http://www.factsandcomparisons.com) or call 800.223.0554.

 **Trial Step and Additional Use of Ontology**

* 11. Physician opens ‘interface’ to view all trials for AD. These are local, national, and international.

Ontology sources :

FDA

WHO

Other that may be freely available and will provide an all-inclusive list of on-going trials?

* 12. Either :
	1. Enroll patient in a clinical trial as one of the agents looks very suitable and may benefit patient, or patient interested
	2. Do not enroll as patient declines, or trials unsuitable
	3. Obtain information for patient, with potential of future enrollment or not depending on best interest of patient.
* 13. Physician checks patient meets inclusion/exclusion criteria through querying their eHR
* 14. Patient has thorough medical (lifestyle assessment, medical history, genomics, proteomics, metabolomics, images, cognition) to supplement and update existing data
* 15. Results of the medical exam influence the arm of the trial in which the patient participates

**Researcher/Industry/Academic Input**

* 16. Segment patients according to those who responded to a drug, those who didn’t, and those who had an adverse drug reaction
* 17. Look to see the variation in response according to the clinical protocol

**Future Direction – use by Academic, Pharma Industry or Clinician**

* 18. Stratify or design a new study using personalized data in Eprofile with patient’s permission
* 19.Use SNP genomic data to
	1. Perfect or focus treatment with agents already in clinical use to make them more patient specific to avoid harmful effects or ensure they are more efficacious
	2. Use data in Phase I for predictive toxicity study and analysis
	3. Use data/receptor status to identify additional targets for drug development

**Additional Important Data Sources :**

OVID

PUBMED

MEDLINE

{To liase and decide how to integrate information listed}

http://www.ncbi.nlm.nih.gov/sites/gquery

http://www.ncbi.nlm.nih.gov/Database/index.html

[*Entrez*](http://www.ncbi.nlm.nih.gov/Entrez/index.html) is the integrated, text-based search and retrieval system used at NCBI for the major databases, including PubMed, Nucleotide and Protein Sequences, Protein Structures, Complete Genomes, Taxonomy, and others. Click on the graphic below for a more detailed view of Entrez integration.

