Webinar Series
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RxNav
Browser and Application Programming Interfaces for Drug Information Sources

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Acknowledgments

- Lee Peters
- Thang Nguyen
- Kelly Zeng
- Ramez Ghazzaoui
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- Kin Wah Fung (RxTerms)
- Mark Erlbaum (NDF-RT)
Outline

◆ **RxNorm**
  - Drug vocabulary integration
  - Drug vocabulary standardization

◆ **Other drug information sources accessible through RxNav**
  - RxTerms
  - NDF-RT

◆ **Visualizing drug information:** RxNav

◆ **Processing drug information:** RxNorm API

◆ Applications
References

- **RxNav and RxNorm APIs**
- **RxNorm**
- **RxTerms**
- **NDF-RT**
RxNorm

Overview
Motivation

- Exchange of information requires standardized names
  - Ordering drugs
  - Checking interactions
  - Inventory management
- No standard naming conventions for drugs
- Integrating drug vocabularies
- Unique identifiers for drugs
- Specify relations among drug entities
Drug vocabulary integration

RxNorm
UMLS-like approach

◆ 11 source vocabularies
◆ Synonymous names grouped into an RxNorm concept
◆ Unique identifiers (RxCUI)
◆ RRF format

◆ Differences
  ● RxNorm creates its own names
  ● Principled use of named relationships
  ● Limited scope: drug names
Source vocabularies in RxNorm

- Gold Standard Alchemy
- Medi-Span Master Drug Data Base
- Multum MediSource Lexicon
- Micromedex RED CODE
- Medical Subject Headings
- FDA National Drug Code Directory
- FDA Structured Product Labels
- First DataBank NDDF Plus
- VHA National Drug File-Ref. Terminology
- SNOMED Clinical Terms (drug information)
- VHA National Drug File

RxNorm

(terms in thousands, as of January 2011)

- 23
- 13
- 66
- 11
- 19
- 86
- 44
- 87
- 133*
- 87*
- 48
- 113
RxNorm concept

Ingredient

Acetaminophen

SNOMED CT
MeSH
Multum
NDDF
...

161

Acetaminophen
Paracetamol
APAP
Paracetamol product
Acetaminophen (product)
Acetaminophen (substance)
Acetaminophen product

MMSL:5005
SNOMEDCT:387517004
SNOMEDCT:90332006
NDDF:001605
MTHSPL:362O9ITL9D
MMSL:4119
MMSL:d00049
VANDF:4017513
MMSL:4992
MMSL:52845
MTHFDA:50612
UMLS: C0000970
Drug vocabulary standardization

RxNorm
Normalization

◆ Lexical level
  ● Conventions for representing names (strength, units, etc.)

◆ Structural level
  ● Conventions for representing types of drug entities and their interrelations
<table>
<thead>
<tr>
<th>Brand</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS</td>
<td>Digoxin 0.25mg/1mL Solution for injection</td>
</tr>
<tr>
<td>GS</td>
<td>Digoxin 500mcg/2mL Solution for injection</td>
</tr>
<tr>
<td>MDDB</td>
<td>Digoxin Inj 0.25 MG/ML</td>
</tr>
<tr>
<td>MMSL</td>
<td>Digoxin 250 mcg/mL (0.25 mg/mL) injectable solution</td>
</tr>
<tr>
<td>MMSL</td>
<td>Digoxin, 250 mcg/mL (0.25 mg/mL) injectable solution</td>
</tr>
<tr>
<td>MMX</td>
<td>Digoxin 0.25 MG/ML Injection Solution</td>
</tr>
<tr>
<td>MTHFDA</td>
<td>DIGOXIN 0.25 MG INTRAMUSCULAR INJECTION, SOLUTION</td>
</tr>
<tr>
<td>MTHFDA</td>
<td>DIGOXIN 250 MCG INTRAMUSCULAR INJECTION</td>
</tr>
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<td>MTHFDA</td>
<td>DIGOXIN 250 MCG INTRAVENOUS INJECTION</td>
</tr>
<tr>
<td>MTHSPL</td>
<td>digoxin 0.25 MILLGRAM In 1.0 MILLILITER INTRAVENOUS INJECTION</td>
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<td>MTHSPL</td>
<td>Digoxin 250 MICROGRAM In 1 MILLILITER INTRAVENOUS INJECTION, SOLUTION</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN 250 mcg/mL INJECTION AMPUL (ML)</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN 250 mcg/mL INJECTION DISPOSABLE SYRINGE (ML)</td>
</tr>
<tr>
<td>NDDF</td>
<td>DIGOXIN@250 mcg/mL@INJECTION@AMPUL (ML)</td>
</tr>
<tr>
<td>SNOMEDCT</td>
<td>Digoxin 250micrograms/mL injection solution 2mL ampule</td>
</tr>
<tr>
<td>SNOMEDCT</td>
<td>Digoxin 500micrograms/2mL injection</td>
</tr>
<tr>
<td>VANDF</td>
<td>DIGOXIN 0.25MG/ML INJ</td>
</tr>
<tr>
<td>[...]</td>
<td>[...]</td>
</tr>
</tbody>
</table>

**Digoxin 0.25 MG/ML Injectable Solution**
Normalization

Structural level

- Structural level
  - Atomic elements
    - Ingredient
    - Strength
    - Dose form
  - Generic vs. Brand names
  - Principle set of relationships among the different types
Dose form

Ingredient

Fluoxetine

Dose form

Ingredient

4mg/ml

Strength

Clinical drug component

Ingredient

Dose form

Clinical drug form

Strength

Clinical drug
Generic vs. Brand

- **Generic**
  - Ingredient (IN)
  - Clinical drug form (SCDF)
  - Clinical drug component (SCDC)
  - Clinical drug (SCD)

- **Brand**
  - Brand name (BN)
  - Branded drug form (SBDF)
  - Branded drug component (SBDC)
  - Branded drug (SBD)

*tradename_of*
Relations among drug entities
Relations among drug entities (revisited)

Ingredient

Azithromycin

C. Drug Component

Azithromycin 250 MG

B. Drug Component

Azithromycin 250 MG

G. Pack

{6 (Azithromycin 250 MG Oral Tablet) } Pack

B. Pack

Z-PAK

B. Drug Form

Azithromycin Oral Tablet

C. Drug Form

Azithromycin Oral Tablet

C. Drug

Azithromycin 250 MG Oral Tablet

B. Drug

Zithromax 250 MG Oral Tablet

Brand Name

Zithromax
RxNorm database

◆ 11 data sources
  - Gold Standard Alchemy
  - Medi-Span Master Drug Data Base
  - Multum MediSource Lexicon
  - Micromedex RED BOOK
  - Medical Subject Headings
  - FDA National Drug Code Directory
  - FDA Structured Product Labels
  - First DataBank NDDF Plus
  - VHA NDF – RT
  - SNOMED Clinical Terms
  - VHA National Drug File

◆ Content
  - 4,942 ingredients
  - 14,667 brand names
  - 19,862 clinical drugs
  - 16,275 branded drugs
  - 307 generic packs
  - 388 branded packs
  - 15,715 clinical drug comp.
  - 14,680 branded drug comp.
  - 8,478 clinical drug forms
  - 12,188 branded drug forms
  - 100 dose forms

(as of January 26, 2011; excluding obsolete data)
Other drug information sources accessible through RxNav

RxTerms
NDF-RT
RxTerms

◆ Drug interface terminology derived from RxNorm for prescription writing or medication history recording
  ● Commonly used synonyms and abbreviations (e.g. HCTZ for hydrochlorothiazide)
  ● “tall man” lettering recommended by FDA to avoid medication errors
    ◆ ChlorproMAZINE
    ◆ ChlorproPAMIDE
◆ Developed at NLM
National Drug File Reference Terminology

- Developed by the Veterans Health Administration
- Part of the VA clinical information system
- Available from the NCI web site (XML, OWL)
- Integrated in RxNorm since June 2010
Clinical information

- Pharmacologic class, Ingredients (isa)
- Therapeutic intent (may_treat, may_diagnose, may_prevent)
- Chemical ingredient (has_ingredient, has_active_metabolites)
- Mechanism of action (has_MoA)
- Physiologic effect (has_PE)
- Pharmacokinetics/Metabolism (has_PK, site_of_metabolism)
- Dose form (has_dose_form)
- Contraindications (CI_with, CI_MoA, CI_PE, induces)
- Drug-drug interactions
NDF-RT Examples

◆ Clopidogrel
  ∙ may_prevent Cerebral Infarction
  ∙ may_prevent Coronary Thrombosis
  ∙ may_prevent Myocardial Infarction
  ∙ CI_with Blood Coagulation Disorders
  ∙ CI_with Drug Hypersensitivity
  ∙ CI_with Hemorrhage
  ∙ has_Ingredient clopidogrel
  ∙ has_MoA G-Protein-linked Receptor Interactions
  ∙ has_PE Decreased Platelet Aggregation

◆ CLOPIDOGREL BISULFATE 75MG TAB,UD
  ∙ isa PLATELET AGGREGATION INHIBITORS
**Pharmaceutical Preparations**

**Drug Products by VA Class**
- BLOOD PRODUCTS /MODIFIERS /VOLUME EXPANDERS
- PLATELET AGGREGATION INHIBITORS

**Drug Products by Generic Ingredient Combinations**
- C [Preparations]
- CLOPIDOGREL
- CLOPIDOGREL BISULFATE
- CLOPIDOGREL BISULFATE 75MG TAB

**External Pharmacologic Classes**
- Anti-coagulant
- Platelet Aggregation Inhibitor

**Legacy VA classes**
- Decreased Coagulation Activity
- Decreased Platelet Aggregation
- Myocardial Infarction
- Hemorrhage

**Representation of the drug Clopidogrel in NDF-RT**

**Legend**
- has PE: has physiologic effect
- CI with: contra-indicated with isa (stated)
Visualizing drug information

RxNav
RxNav

◆ Visualization and navigation
  - RxNorm browser
    - Integrated with RxTerms and NDF-RT
  - Auto-completion and spelling correction
  - Search on names and codes (including proprietary)
  - Standalone application
  - Queries databases at NLM (RxNorm, RxTerms, NDF-RT)
  - Links to external sources (DailyMed)

◆ Drug information processing
  - API to the RxNorm database
  - Web services (SOAP, REST)
RxNav demo

http://rxnav.nlm.nih.gov/
<table>
<thead>
<tr>
<th>Attribute</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RxNorm Name</td>
<td>clopidogrel 75 MG Oral Tablet</td>
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<tr>
<td>RxCUI</td>
<td>309362</td>
</tr>
<tr>
<td>TTY</td>
<td>SCD</td>
</tr>
<tr>
<td>UMLSCUI</td>
<td>C0976741</td>
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<td>Master Drug Data Base</td>
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<td>Multum MEDISOURCE Lexicon</td>
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<td>Source</td>
<td>MetaThesaurus FDA Structured Product Labels</td>
</tr>
<tr>
<td>Source</td>
<td>National Drug Data File Plus Source Vocabulary</td>
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<tr>
<td>Source</td>
<td>National Drug File</td>
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<tr>
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<td>SNOMED Clinical Terms</td>
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<td>Source</td>
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RxCUI: 309362
Name: clopidagrel 75 MG Oral Tablet

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**Properties Table**

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<td>CLOPIDOGREL BISULFATE 75MG TAB,UD</td>
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<tr>
<td>kind</td>
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<tr>
<td>Level</td>
<td>VA Product</td>
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<td>Active</td>
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<td>Units</td>
<td>MG</td>
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<td>C0975741</td>
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<td>RxNorm_CUI</td>
<td>309362</td>
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<td>RxNorm_Name</td>
<td>clopidogrel 75 MG Oral Tablet</td>
</tr>
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</tr>
<tr>
<td>VA_National_For</td>
<td>CLOPIDOGREL TAB</td>
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<tr>
<td>Kind</td>
<td>Subject</td>
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<td>--------------</td>
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<td>CLOPIDOGREL BISULFATE 75MG TAB, UD</td>
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<tr>
<td>Disease</td>
<td>CLOPIDOGREL</td>
</tr>
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<td>CLOPIDOGREL</td>
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<tr>
<td>Disease</td>
<td>CLOPIDOGREL</td>
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<td>Dose Form</td>
<td>CLOPIDOGREL BISULFATE 75MG TAB, UD</td>
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<td>Ingredient</td>
<td>CLOPIDOGREL</td>
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<td>Mechanism of A...</td>
<td>CLOPIDOGREL</td>
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<tr>
<td>Physiologic Effect</td>
<td>CLOPIDOGREL</td>
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</table>
CLOPIDOGREL BISULFATE 75MG TAB,UD

Drug

Pharmaceutical Preparations

Drug Products by Generic Ingredient Combinations

Drug Products by VA Class

C [Preparations]

BLOOD PRODUCTS/MODIFIERS/VOLUME EXPANDERS

PLATELET AGGREGATION INHIBITORS

CLOPIDOGREL

CLOPIDOGREL BISULFATE

CLOPIDOGREL BISULFATE 75MG TAB,UD

Legend

VA Class

VA Product

DRUG

association

DRUG
CLOPIDOGREL BISULFATE 75MG TAB,UD
Pharmacokinetics
CLOPIDOGREL BISULFATE 75MG TAB,UD

Drug Interactions

CIMETIDINE [Significant]
OMEPRAZOLE [Significant]
WARFARIN [Significant]
Processing drug information

RxNorm Application Programming Interface
RxNorm APIs

- Made available in March 2008
- Based on Web Services
  - SOAP, REST
    - Independent of any programming language
- Used by *RxNav* and other applications
- Enable access to all information displayed in RxNav

Documentation


Testing environment (SOAP client demo)

List of functions (SOAP) 1/3

◆ Housekeeping functions
  • getRxNormVersion()
  • getIdTypes()
  • getRelaTypes()
  • getTermTypes()
  • getSourceTypes()

◆ Find RxNorm concepts
  • By name: findRxcuiByString( searchString, source-list, allSourcesFlag, searchType )
  • By code: findRxcuiById( idType, id, allSourcesFlag )
  • Help: getSpellingSuggestions( searchString )
  • Versioning: findRemapped( rxcui )
Get RxNorm concept properties

- `getRxConceptProperties( rxcui )`
- `getStrength( rxcui )`
- `getQuantity( rxcui )`
- `getNDCs( rxcui )`
- `getUNII( rxcui )`
- `getProprietaryInformation( rxcui, source-list, proxyTicket* )`
List of functions (SOAP) 3/3

◆ Get RxNorm concept relations
  • By rel.: getRelatedByRelationship( rxcui, rel-list )
  • By type: getRelatedByType( rxcui, type-list )
  • All: getAllRelatedInfo( rxcui )

◆ Miscellaneous functions
  • getDrugs( name )
  • getDisplayTerms()
  • getMultiIngredBrand( rxcui-list )
Documentation

✦ Java

```java
import java.net.URL;
import BeanService.*;
import gov.nih.nlm.mor.axis.services.RxNormDBService.*;

String rxhost = "http://mor.nlm.nih.gov";
String rxURI = rxhost + "/axis/services/RxNormDBService";

// Locate the RxNorm API web service
URL rxURL = new URL(rxURI);
DBManagerService rxnormService = new DBManagerServiceLocator();
DBManager dbmanager = rxnormService.getRxNormDBService(rxURL);
```
Implementation Perl client

http://mor.nlm.nih.gov/perl/rxnav_api_demo.pl
Implementation .NET client

![RxNorm API access window with method 'getRxConceptProperties (rxcui)', argument 1 '58930', and returned data including 'STR= Zyrtec', 'RXCUI= 58930', 'TTY= BN', 'LAT= ENG', 'SUPPRESS= N', 'SY= ', 'CUI= C0162723']
RESTful API

◆ Base URI
  ● http://rxnav.nlm.nih.gov/REST/

◆ List of resources
  ● http://rxnav.nlm.nih.gov/RxNormRestAPI.html
<table>
<thead>
<tr>
<th>RESTful resource</th>
<th>SOAP-based function</th>
</tr>
</thead>
<tbody>
<tr>
<td>/version</td>
<td>getRxNormVersion</td>
</tr>
<tr>
<td>/displaynames</td>
<td>getDisplayNames</td>
</tr>
<tr>
<td>/idtypes</td>
<td>getIdTypes</td>
</tr>
<tr>
<td>/relatetypes</td>
<td>getRelaTypes</td>
</tr>
<tr>
<td>/termtypes</td>
<td>getTermTypes</td>
</tr>
<tr>
<td>/rxcui?name=value&amp;srclst=value&amp;allsrc=value&amp;search=value</td>
<td>findRxcuiByString</td>
</tr>
<tr>
<td>/rxcui?idtype=value&amp;id=value&amp;allsrc=value</td>
<td>findRxcuiByld</td>
</tr>
<tr>
<td>/rxcui/{rxcui}</td>
<td>(none)</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/properties</td>
<td>getRxConceptProperties</td>
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<tr>
<td>/rxcui/{rxcui}/ndcs</td>
<td>getNDCs</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/allrelated</td>
<td>getAllRelatedInfo</td>
</tr>
<tr>
<td>/rxcui/{rxcui}/related?tty=values</td>
<td>getRelatedByType</td>
</tr>
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<td>/rxcui/{rxcui}/related?rela=values</td>
<td>getRelatedByRelationship</td>
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<td>getQuantity</td>
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<td>getStrength</td>
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<tr>
<td>/rxcui/{rxcui}/proprietary?srclist=values&amp;ticket=value</td>
<td>getProprietaryInformation</td>
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<td>/spellingsuggestions?name=value</td>
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<td>/brands?ingredientids=value</td>
<td>getMultiIngredBrand</td>
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<tr>
<td>/drugs?name=value</td>
<td>getDrugs</td>
</tr>
</tbody>
</table>
REST output XML


```
<?xml version="1.0" encoding="UTF-8" standalone="yes"?>
<rxnormdata>
  <idGroup>
    <name>bactrim</name>
    <rxcui>151399</rxcui>
  </idGroup>
</rxnormdata>
```
REST output  JSON


```
{
    "idGroup" : {
        "rxcui" : "151399",
        "name" : "bactrim"
    }
}
```
Recently released

- Managing variation in clinical drug names
- Use case: mapping of local formularies to RxNorm
- Extends the UMLS program \textit{norm}
- Specific normalization rules
  - Expansion of abbreviations (e.g., tab to tablet)
  - Reformatting of specific elements (e.g., space between number and unit)
  - Removal of salt variants (e.g., succinate from metoprolol succinate)
New functions Coming up soon

◆ **RxMap**
  - Mapping lists of drug names / identifiers to RxNorm
  - Batch mode version of
    - `findRxcuiByString()`
    - `findRxcuiById()`

◆ **RxXMap**
  - Mapping across vocabularies through RxNorm
  - Combines
    - `findRxcuiById()`
    - `getProprietaryInformation()`
  - Requires UMLS license
New APIs  Coming up soon

◆ **RxTerms**
  - SOAP + REST
  - List of RxTerms properties for a given RxCUI

◆ **NDF-RT**
  - SOAP + REST
  - Find NDF-RT entity by name, NUI, RxCUI
  - Get properties for a given NDF-RT drug entity
  - Get relations for a given NDF-RT drug entity
  - Find drug interactions
Applications
Examples of application

◆ Terminology integration and standardization (RxNorm) enables interoperability and mapping across vocabularies

◆ Specific applications
  - Information exchange (“meaningful use”)
  - Medication lists
  - Medication reconciliation
  - E-prescribing / CPOE
  - CDA R2
  - Personal Health Record
Quality control in RxNorm

◆ Multiple equivalent paths between RxNorm entities

getRelatedByRelationship(\(r; \text{consists of}\)) \circ getRelatedByRelationship(\(*; \text{has ingredient}\))

\(?\equiv\)

getRelatedByRelationship(\(r; \text{inverse isa}\)) \circ getRelatedByRelationship(\(*; \text{has ingredient}\))
Examples of application

◆ Quality control in RxNorm: Results
  ● 35,000 pairs of paths investigated
  ● Few discrepancies detected
  ● Types of errors
    ▪ Obsolete brand names
    ▪ Obsolete branded drug forms
    ▪ Erroneous relations
  ● Discrepancies reported to the RxNorm team

[Peters, JAMIA 2009]
Applications outside NLM

◆ RxSafe (OHSU)
  ● “improve medication safety for patients”
  ● http://www.ohsu.edu/RxSafe/

◆ My-Medi-Health (Vanderbilt)
  ● “Child-Centered Medication Management”
Usage statistics  All queries

Number of queries per month

- all queries
- REST queries
- 12 m sliding avg
Usage statistics  Interactive queries

Number of interactive queries per month

- Number of interactive queries increases over time.
- The graph shows a 12-month sliding view of the data.
- The x-axis represents months from Jan-08 to Dec-10.
- The y-axis represents the number of queries from 0 to 10,000.

Legend:
- 12 m sliding...