



New York State  
Center of Excellence in  
Bioinformatics & Life Sciences



Core Curriculum in Clinical and Translational Research Seminar Series  
Biomedical Informatics Series Part 3 of 4



# Pain and Mental Health: A Case Study in Information-Driven Research

February 22, 2012 – Roswell Park Cancer Institute, Buffalo NY

**Werner CEUSTERS, MD**

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and  
Department of Psychiatry*

*University at Buffalo, NY, USA*

*<http://www.org.buffalo.edu/RTU>*



## Overview

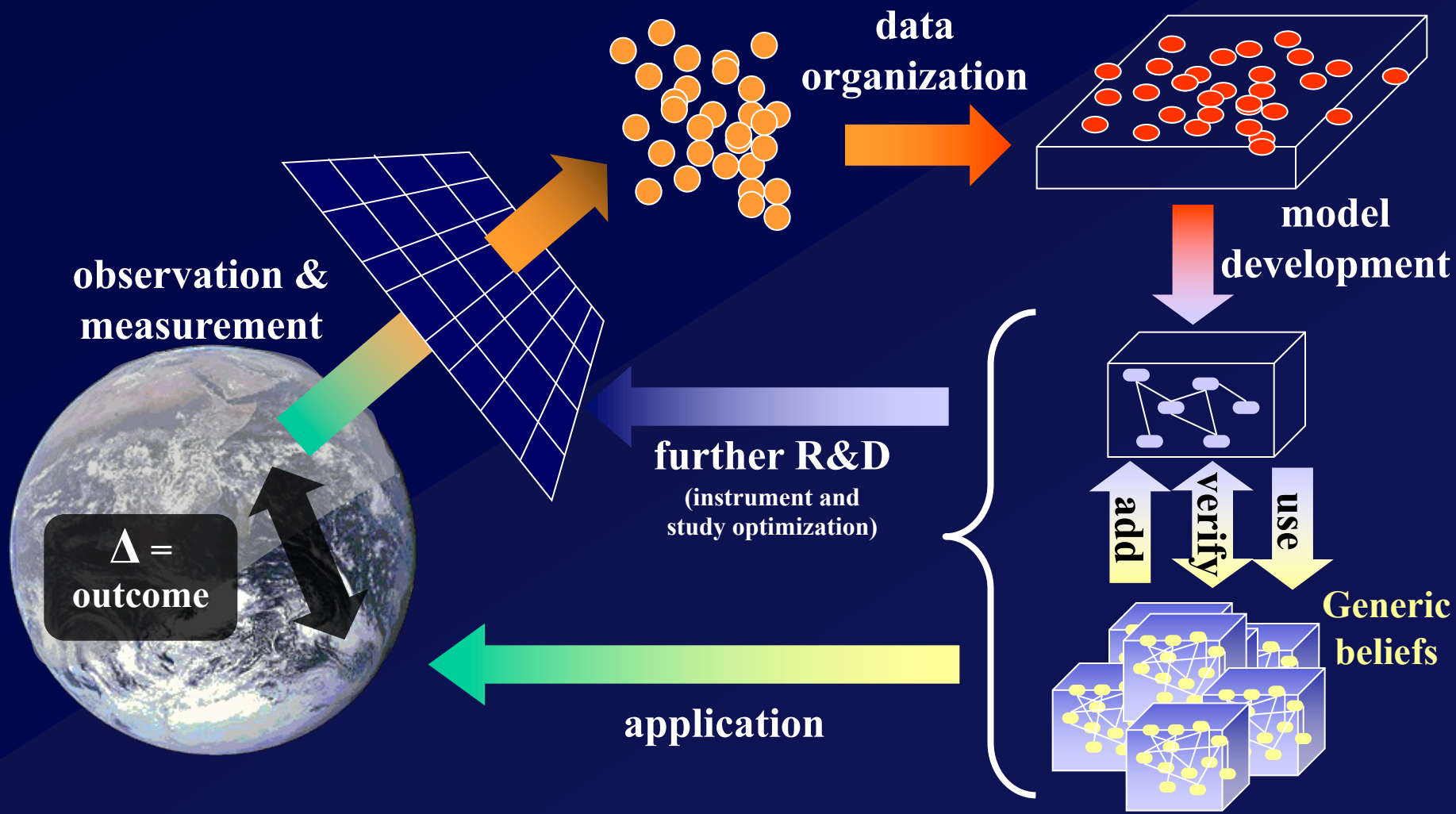
- Principles of data collection
- Introduction to OPMQoL: an ontology for pain-related disablement, mental health and quality of life,
- Making individual data collections more useful for international research,
- Introduction to application ontology building in for OPMQoL.



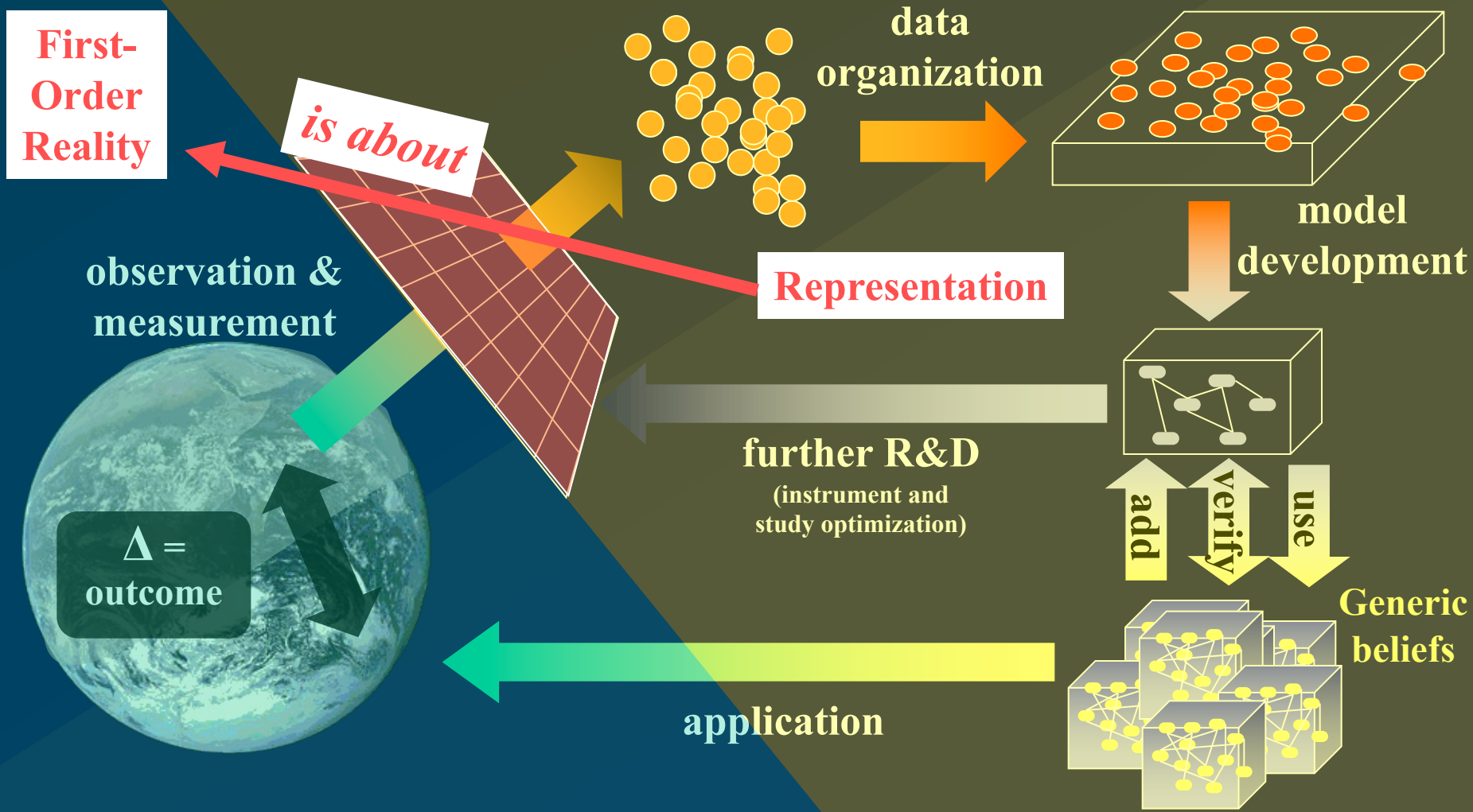
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# Principles of Data Collection

## Data generation and use

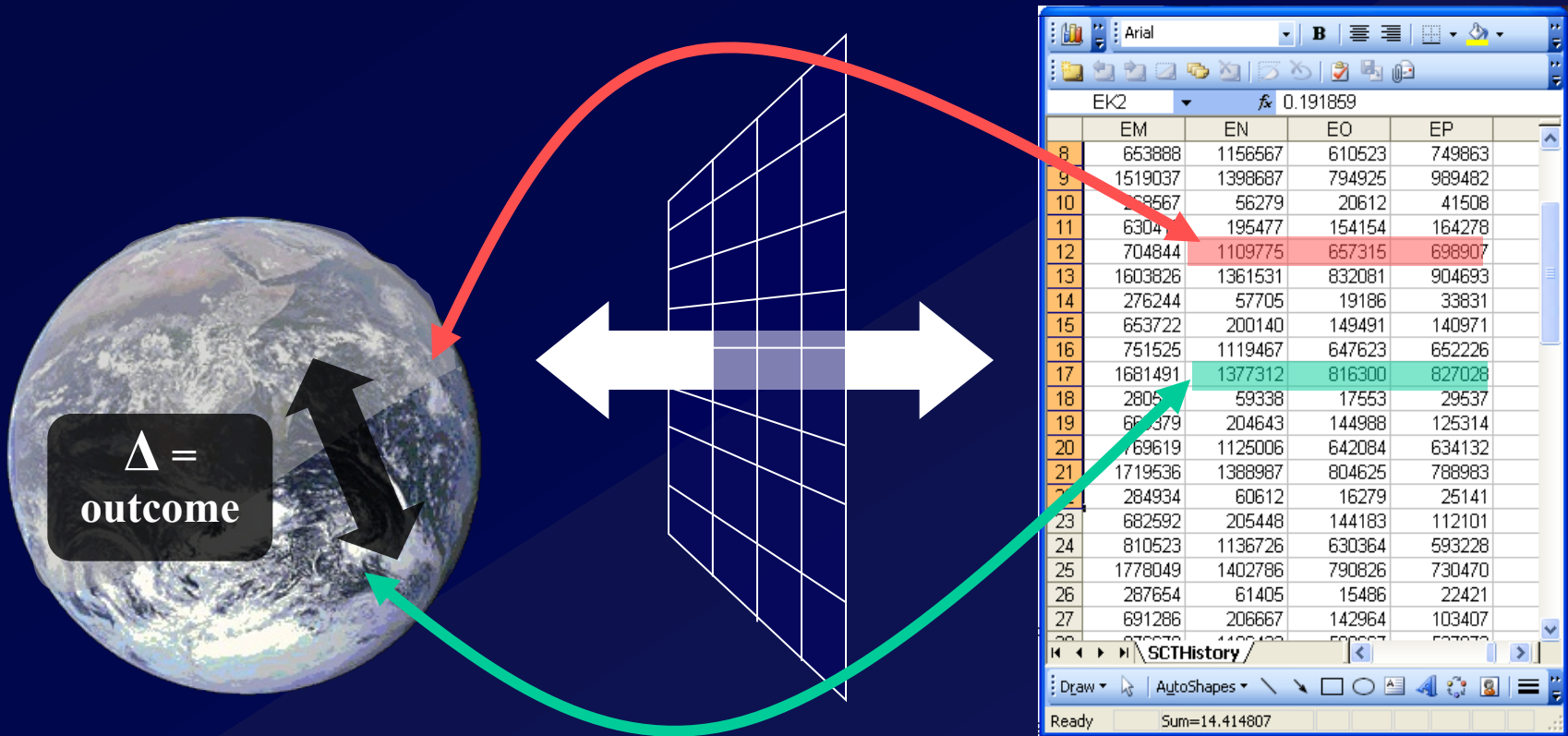


## A crucial distinction: data and what they are about





**Data must be unambiguous and faithful to reality ...**



**Referents**

**References organized  
in a data collection**

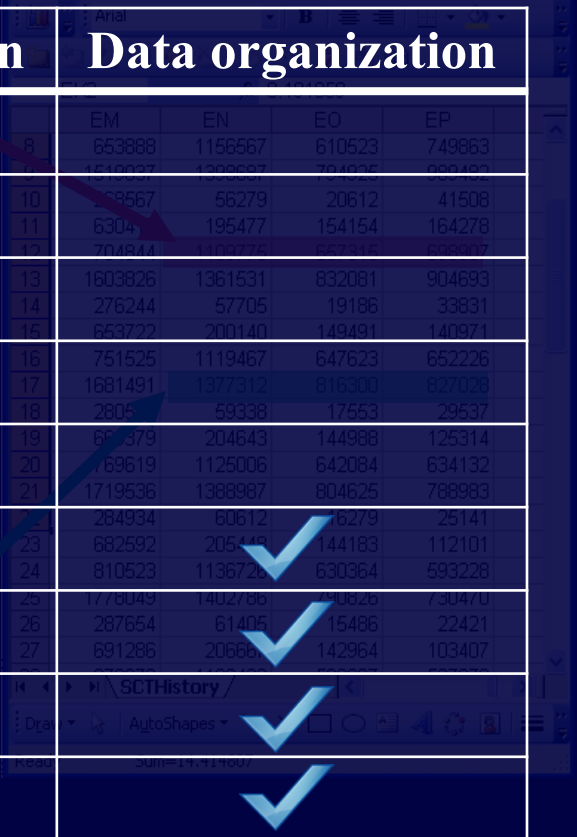
## ... even when reality changes



	EM	EN	EO	EP
8	653888	1156567	610523	749863
9	151937	1388887	794535	984482
10	138887	56279	20612	41508
11	6304	195477	154154	164278
12	704844	1189775	657315	669987
13	1618326	136131	830381	904693
14	276244	57705	19186	33631
15	653722	200140	149491	140971
16	751525	1119467	647523	652226
17	181491	137912	816300	870708
18	286536	59338	17553	25537
19	668379	204643	144888	125314
20	768619	1125005	642084	634132
21	1715636	1388887	804635	788883
22	284934	60612	16279	25141
23	682592	205448	144183	112101
24	810523	1136726	630364	593228
25	1778048	1402786	79836	730470
26	287654	61465	15486	22421
27	691286	206667	142564	103407

- Are differences in data about the same entities in reality at different points in time due to:
  - changes in first-order reality ?
  - changes in our understanding of reality ?
  - inaccurate observations ?
  - registration mistakes ?

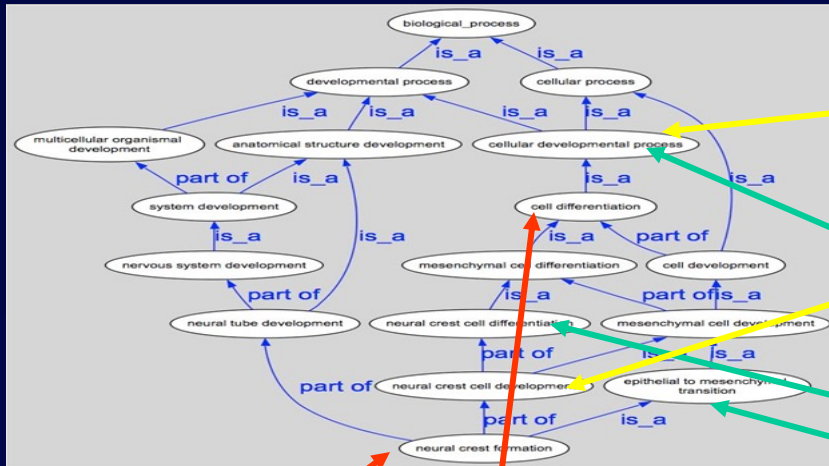
## Methods to achieve faithfulness and data clarity

Sources	Data generation	Data organization
Data collection sheets	✓	
Instruction manuals	✓	
Interpretation criteria	✓	
Diagnostic criteria	✓	
Assessment instruments	✓	
Terminologies	✓	
Data validation procedures	✓	
Data dictionaries		✓
Ontologies	✓	✓

If not used for data collection and organization, these sources can be used post hoc to document, and perhaps increase, the level of data clarity and faithfulness in and comparability of existing data collections.



# Ontologies to make data collections comparable



Cases	Characteristics						
	ch1	ch2	ch3	ch4	ch5	ch6	...
case1							
case2							
case3							
case4							
case5							
case6							
...							

Cases	Characteristics						
	ch1	ch2	ch3	ch4	ch5	ch6	...
case1							
case2							
case3							
case4							
case5							
case6							
...							

Cases	Characteristics						
	ch1	ch2	ch3	ch4	ch5	ch6	...
case1							
case2							
case3							
case4							
case5							
case6							
...							

Linking the variables of distinct data collections  
to a realism-based ontology.



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# **OPMQoL: an Ontology for pain-related disablement, mental health and quality of life**



## Acknowledgement

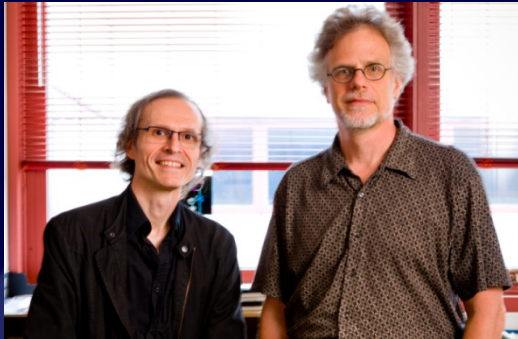
The work described is funded in part by  
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Craniofacial Research (NIDCR). The content of  
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## Collaborators



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Malmö, Sweden



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Hadassah, Israel





## Background (1)

- July 2008, Toronto:
  - the International RDC/TMD Consortium Network identified **a need to incorporate the RDC/TMD diagnostic taxonomy into a comprehensive orofacial pain taxonomy.**
- April, 2009, Miami:
  - ‘The International Consensus Workshop: Convergence on an Orofacial Pain Taxonomy’ participants decided that an adequate treatment of **the ontology of pain in general, and orofacial pain in particular, together with an appropriate terminology, is mandatory to advance the state of the art in diagnosis, treatment and prevention.**



## Background (2)

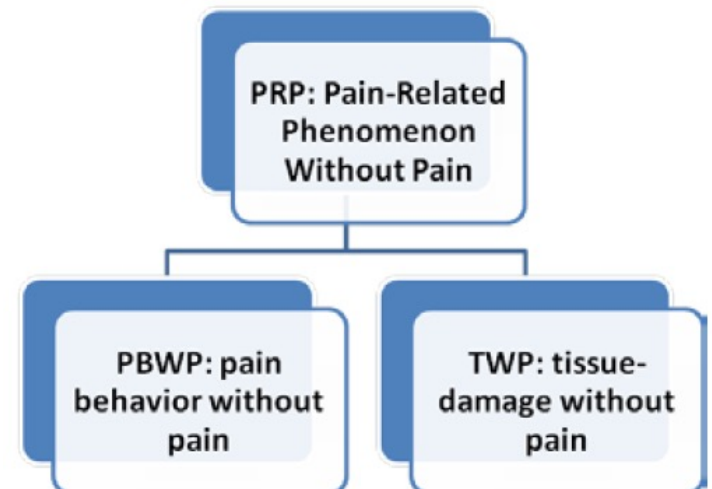
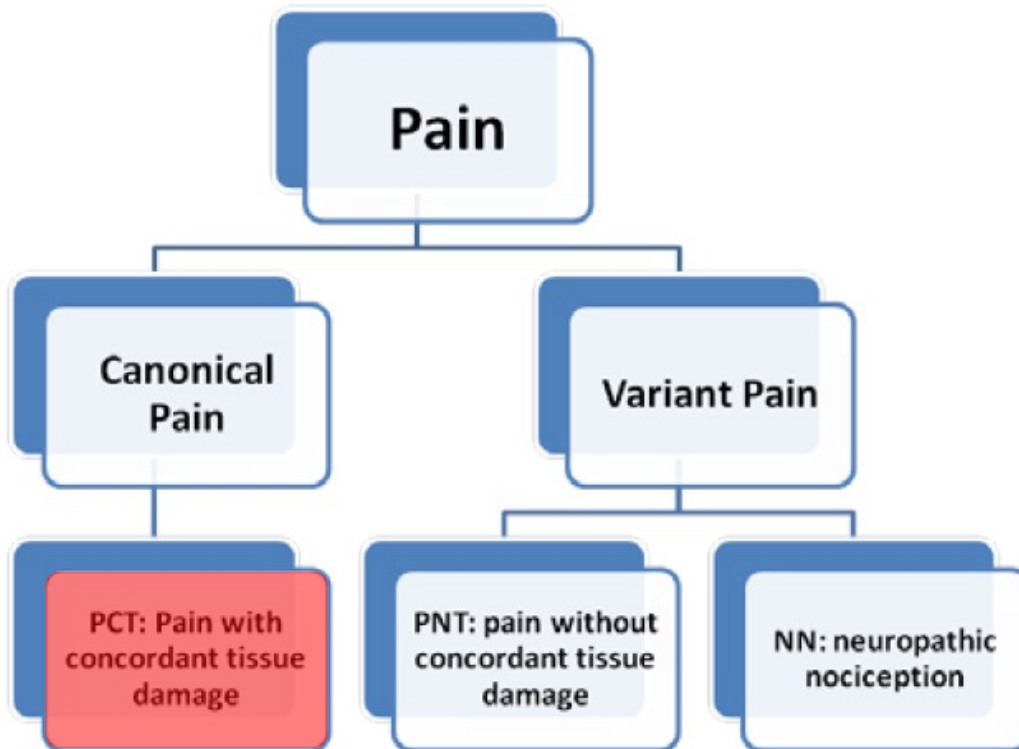
- The following consecutive steps were proposed:
  1. study the terminology and ontology of pain as currently defined,
  2. find ways to make individual data collections more useful for international research,
  3. develop an ontology for integrating knowledge and data over all the known basic and clinical science domains concerning TMD and its relationship to complex disorders, and
  4. expand this ontology to cover all pain-related disorders.



## Study the terminology of pain as currently defined

- Starting point - the IASP definition for ‘pain’:
  - *‘an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage’;*
- what asserts:
  - a common phenomenology (‘unpleasant sensory and emotional experience’) to all instances of pain,
  - the recognition of three distinct subtypes of pain involving, respectively:
    1. actual tissue damage,
    2. what is called ‘potential tissue damage’, and
    3. a description involving reference to tissue damage whether or not there is such damage.

## Results of the ontological analysis



Smith B, Ceusters W, Goldberg LJ, Ohrbach R. Towards an Ontology of Pain. In: Mitsu Okada (ed.), Proceedings of the Conference on Logic and Ontology, Tokyo: Keio University Press, February 2011:23-32.

For ontological definitions  
of these types, see:

[http://www.referent-tracking.com/RTU/sendfile/?file=painTokyo1\\_27\\_2011.pdf](http://www.referent-tracking.com/RTU/sendfile/?file=painTokyo1_27_2011.pdf)  
<http://www.referent-tracking.com/RTU/sendfile/?file=201201PainProject.ppt>





## Main topics for this lecture

- The following consecutive steps were proposed:
  1. study the terminology and ontology of pain as currently defined,
  2. find ways to make individual data collections more useful for international research,
  3. develop an ontology for integrating knowledge and data over all the known basic and clinical science domains concerning TMD and its relationship to complex disorders, and
  4. expand this ontology to cover all pain-related disorders.



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**Find ways to make individual data  
collections more useful for  
international research**



## Methodology

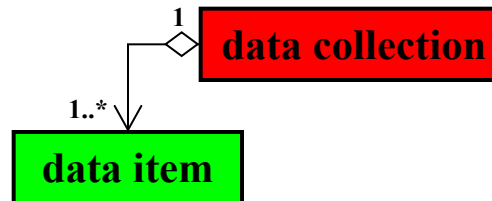
- For data collections still to be generated:
  - express all study criteria, variables and possible values in terms of realism-based ontologies
- For existing data collections:
  - analyze data dictionaries, assessment instruments, study criteria and corresponding terminologies,
  - build realism-based application ontologies to link these sources to realism-based reference ontologies.



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A data collection consists of at least 1 data item, each data item belonging to exactly 1 collection

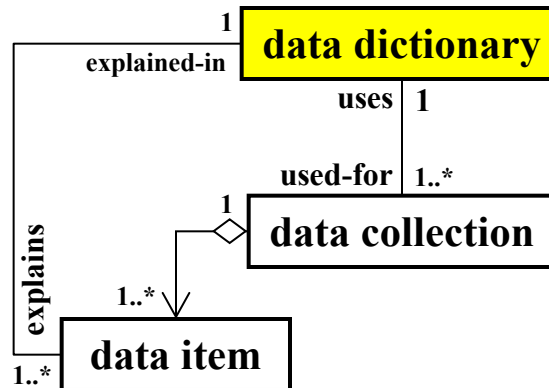
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14	276244	57705	19186	33831
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17	1681491	1377312	816300	827028
18	280538	59338	17553	29537
19	669379	204643	144988	125314
20	769619	1125006	642084	634132
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24	810523	1136726	630364	593228
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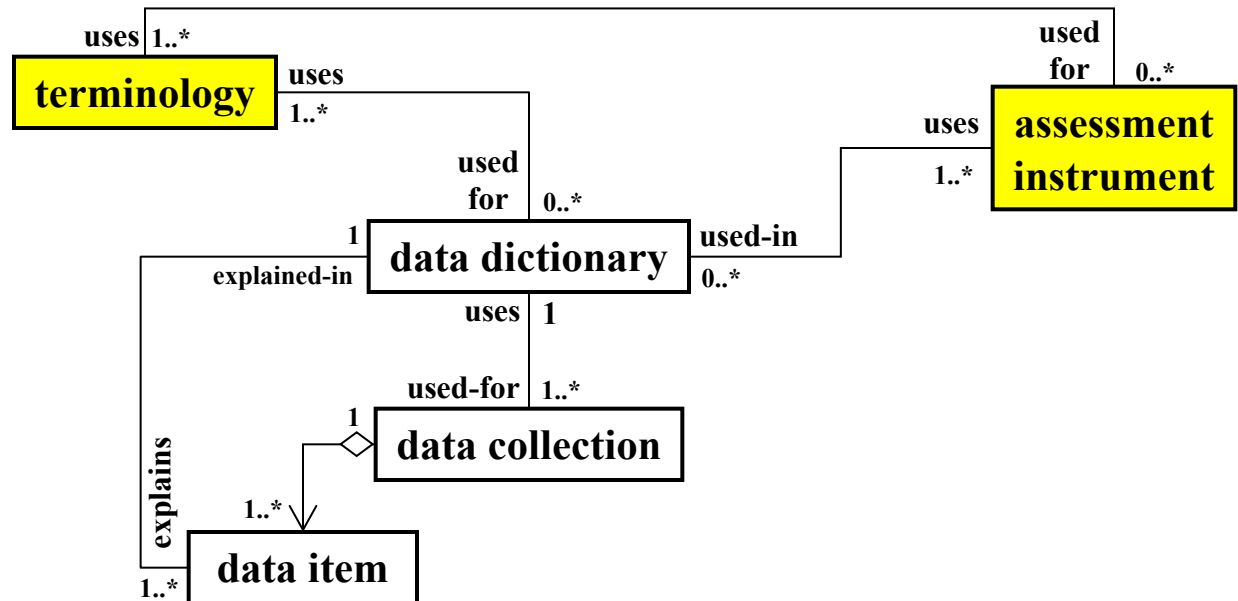


**Data dictionaries provide information about data items and data collections**





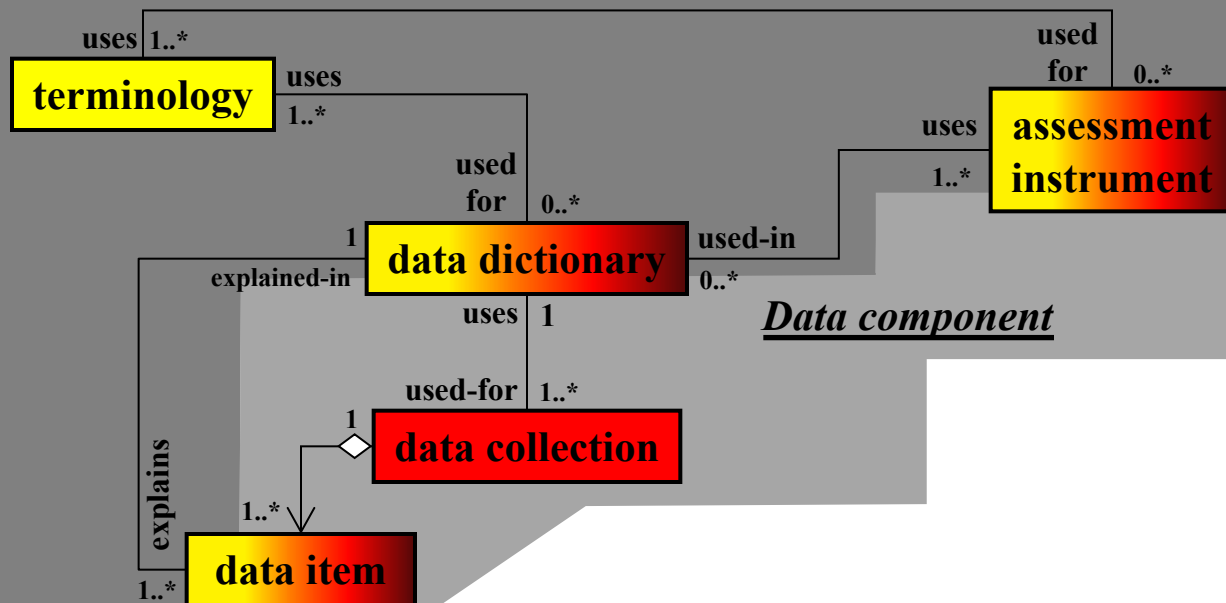
Data dictionaries provide also information about terminologies and assessment instruments used for data generation, in addition to information about the collection's structure





## Relation of Terminology component to Data component

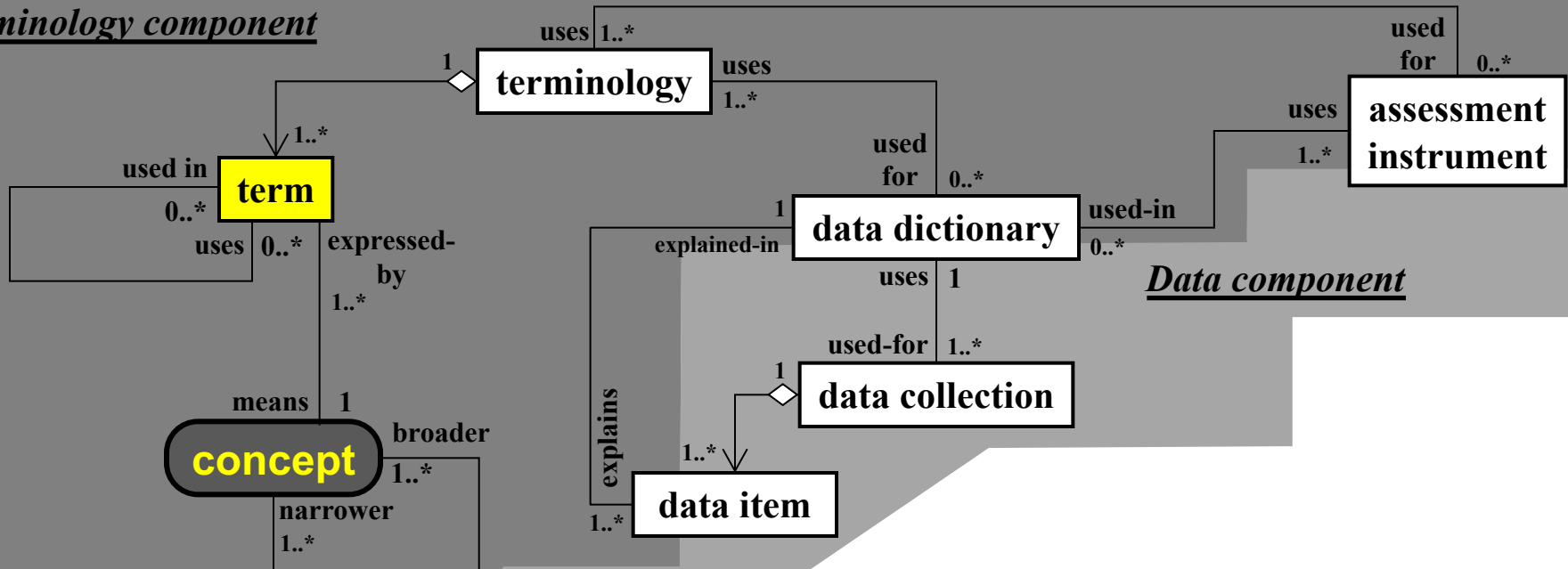
### Terminology component



### Data component

## Terminology links terms to ‘*concepts*’

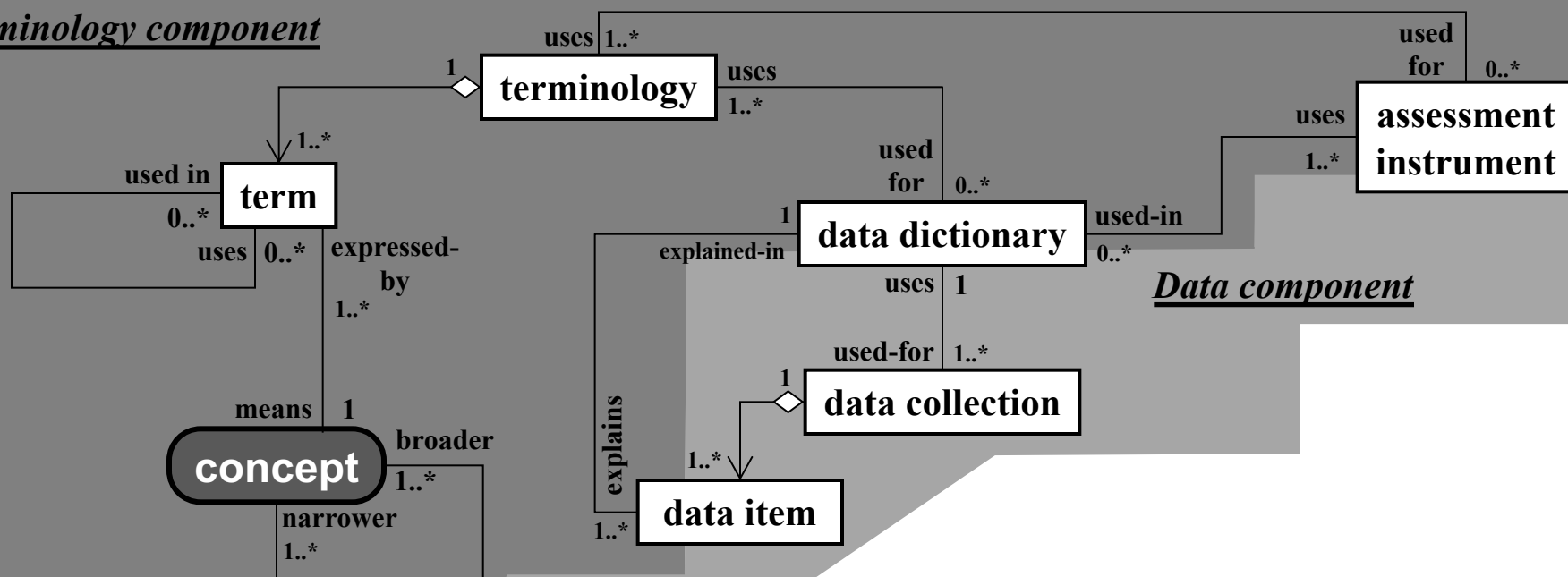
### Terminology component





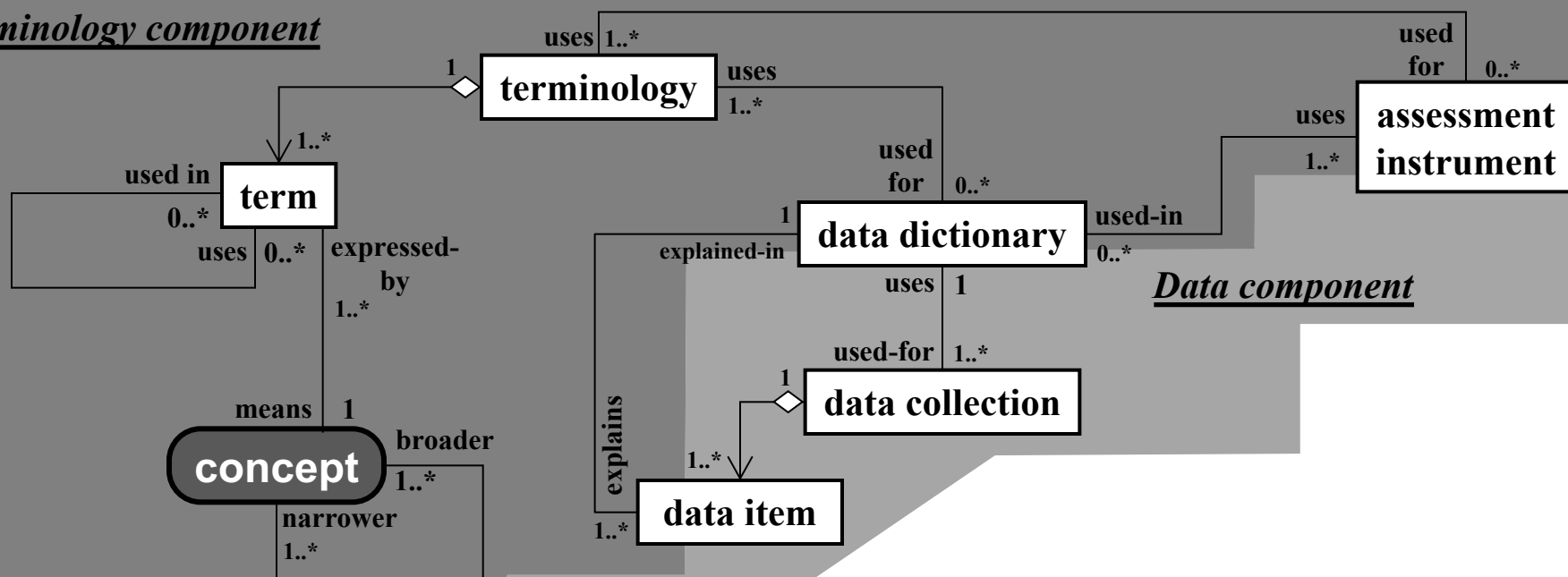
## Not 'concepts' are of interest, but entities in reality

### Terminology component



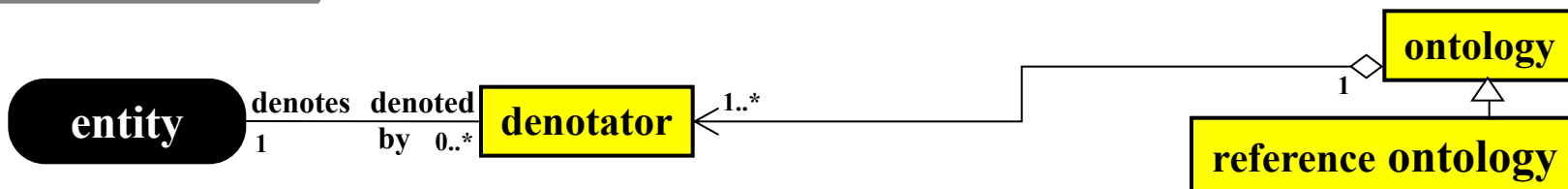
## It is real entities that should be denoted in ontologies

### Terminology component



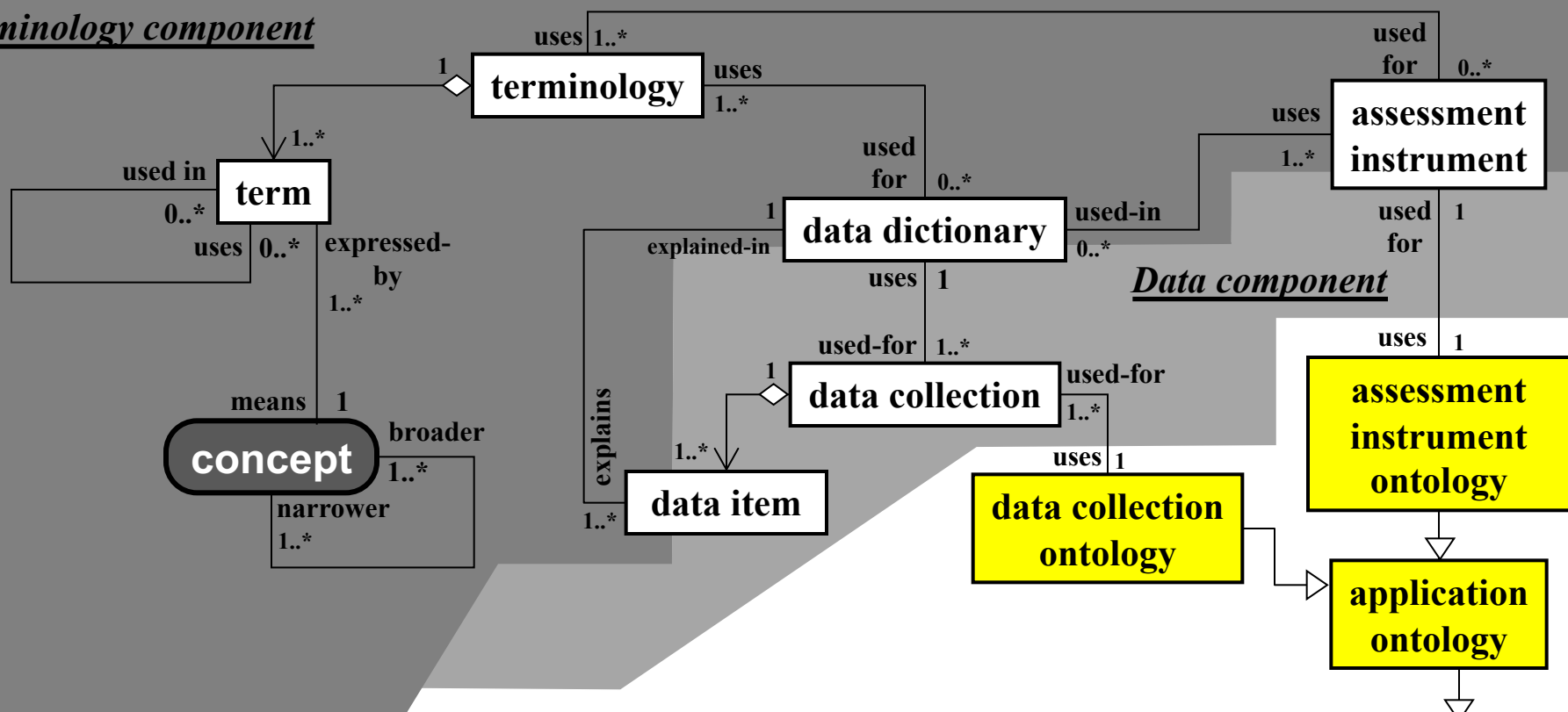
### Data component

### Ontology component

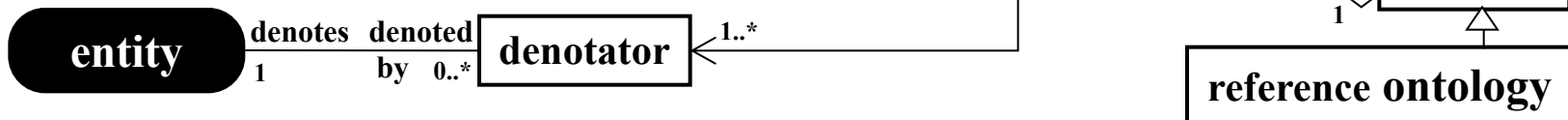


## Application ontologies cover the domains of the sources

### Terminology component

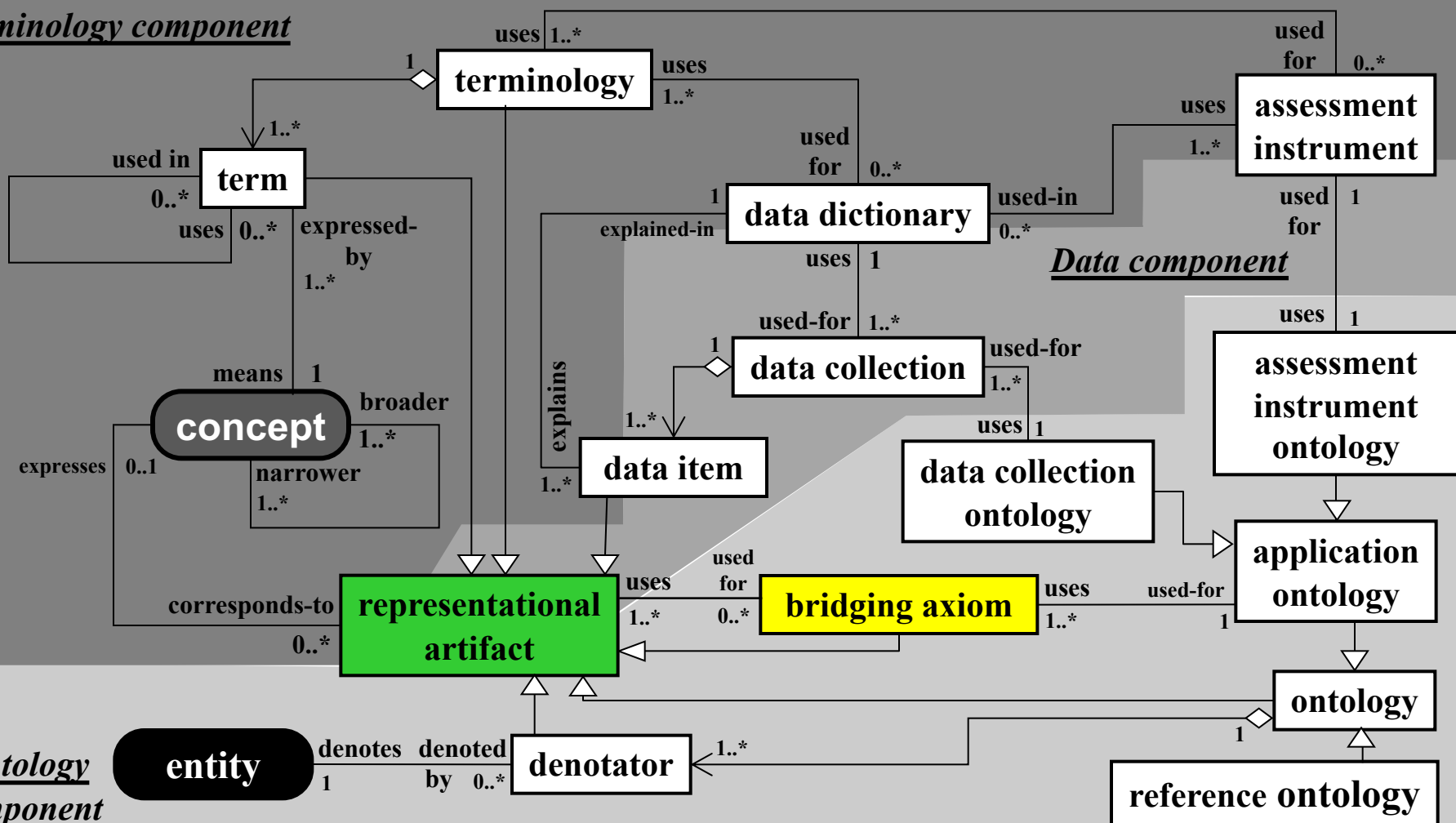


### Ontology component



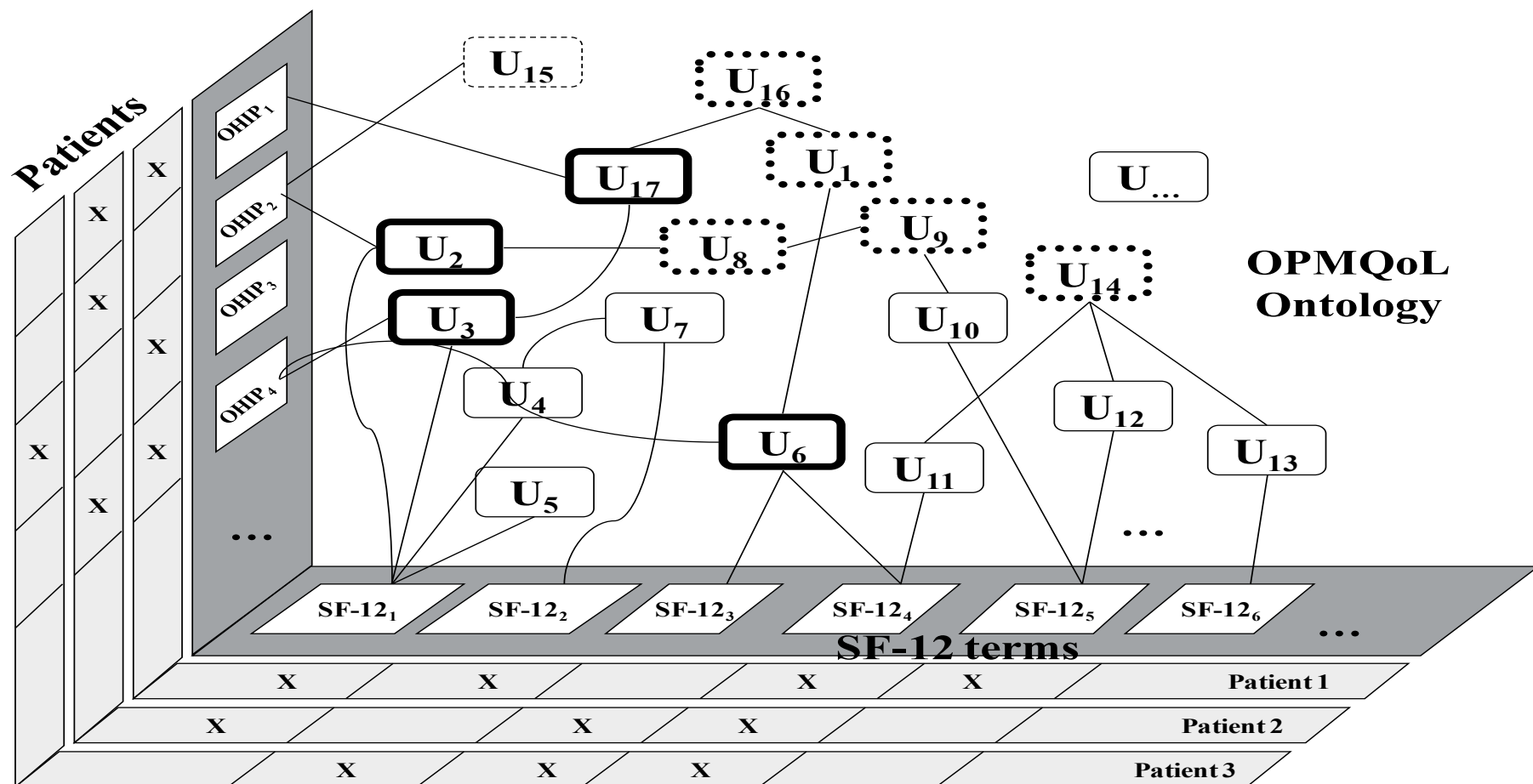
## Bridging axioms link data to ontologies and terminologies

### Terminology component



## Linking data collections using distinct assessment instruments

**OHIP terms**



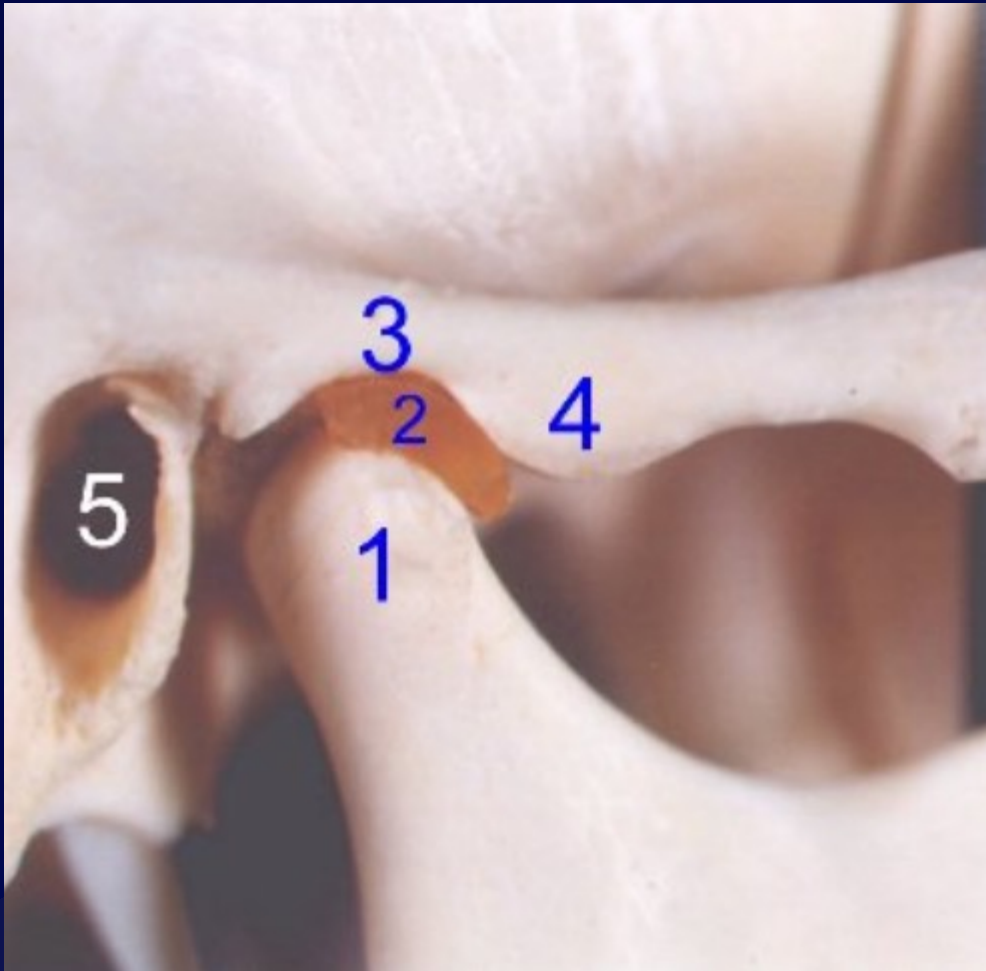




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## Detailed example of the ontology building procedure

## Example: assessing TMJ Anatomy



### Temporomandibular Joint (TMJ)

1. Mandibular condyle
2. Articular disk
3. Superior joint cavity
4. Articular eminence
5. External ear



## Panoramic X-ray of mouth





# Hard Tissue Assessment: Panoramic X-ray

## I. TMJ Finding(s)

### Right TMJ

#### A) Condylar Head

- ☐ N ☐ Y Gross Hypoplasia
- ☐ N ☐ Y Gross Hyperplasia
- ☐ N ☐ Y Flattening
- ☐ N ☐ Y Subcortical Sclerosis
- ☐ N ☐ Y Subcortical Cyst
- ☐ N ☐ Y Surface Erosion
- ☐ N ☐ Y Osteophyte
- ☐ N ☐ Y Generalized Sclerosis
- ☐ N ☐ Y Loose Joint Bodies
- ☐ N ☐ Y Deviation in Form

#### B) Fossa/Eminence

- ☐ N ☐ Y Flattening
- ☐ N ☐ Y Subcortical Sclerosis
- ☐ N ☐ Y Surface Erosion

#### C) Diagnosis

- ☐ 1 Normal
- ☐ 2 Indeterminant
- ☐ 3 Osteoarthritis
- ☐ 4 Other (List):

#### D) Miscellaneous

- ☐ N ☐ Y Ankylosis





## RDC/TMD: a collaborator's data dictionary

**Hard Tissue Assessment: Panoramic X-ray**

**I. TMJ Finding(s)**

**Right TMJ**

**A) Condylar Head**

☐ ☐ Gross Hypoplasia

☐ ☐ Gross Hyperplasia

☐ ☐ Flattening

☐ ☐ Subcortical Sclerosis

☐ ☐ Subcortical Cyst

☐ ☐ Surface Erosion

☐ ☐ Osteophyte

☐ ☐ Generalized Sclerosis

☐ ☐ Loose Joint Bodies

☐ ☐ Deviation in Form

**B) Fossa/Eminence**

☐ ☐ Flattening

☐ ☐ Subcortical Sclerosis

☐ ☐ Surface Erosion

**C) Diagnosis**

☐ Normal

☐ Indeterminant

☐ Osteoarthritis

☐ Other (List):

**D) Miscellaneous**

☐ ☐ Ankylosis

**I. TMJ Finding(s)**

**A. Right TMJ**

PanRtIA1	
PanRtIA2	
PanRtIA3	
PanRtIA4	
PanRtIA5	
PanRtIA6	
PanRtIA7	
PanRtIA8	
PanRtIA9	
PanRtIA10	

0 - No  
1 - Yes  
9 - missing

Gross Hypoplasia  
Gross Hyperplasia  
Flattening  
Subcortical Sclerosis  
Subcortical Cyst  
Surface Erosion  
Osteophyte  
Generalized Sclerosis  
Loose Joint Bodies  
Deviation in Form

Fieldnames in  
Eric's data  
collection

Allowed values for  
the fields





## Anybody sees something disturbing ?

### Hard Tissue Assessment: Panoramic X-ray

#### I. TMJ Finding(s)

##### Right TMJ

##### A) Condylar Head

- ☐ Gross Hypoplasia
- ☐ Gross Hyperplasia
- ☐ Flattening
- ☐ Subcortical Sclerosis
- ☐ Subcortical Cyst
- ☐ Surface Erosion
- ☐ Osteophyte
- ☐ Generalized Sclerosis
- ☐ Loose Joint Bodies
- ☐ Deviation in Form

##### B) Fossa/Eminence

- ☐ Flattening
- ☐ Subcortical Sclerosis
- ☐ Surface Erosion

##### C) Diagnosis

- ☐ Normal
- ☐ Indeterminant
- ☐ Osteoarthritis
- ☐ Other (List):

##### D) Miscellaneous

- ☐ Ankylosis

#### I. TMJ Finding(s)

##### A. Right TMJ

PanRtIA1	
PanRtIA2	
PanRtIA3	
PanRtIA4	
PanRtIA5	
PanRtIA6	
PanRtIA7	
PanRtIA8	
PanRtIA9	
PanRtIA10	

0 - No

1 - Yes

9 - missing

Gross Hypoplasia  
Gross Hyperplasia  
Flattening  
Subcortical Sclerosis  
Subcortical Cyst  
Surface Erosion  
Osteophyte  
Generalized Sclerosis  
Loose Joint Bodies  
Deviation in Form



## This data dictionary alone is not reliable!

### Hard Tissue Assessment: Panoramic X-ray

#### I. TMJ Finding(s)

##### Right TMJ

##### A) Condylar Head

- ☐ Gross Hypoplasia
- ☐ Gross Hyperplasia
- ☐ Flattening
- ☐ Subcortical Sclerosis
- ☐ Subcortical Cyst
- ☐ Surface Erosion
- ☐ Osteophyte
- ☐ Generalized Sclerosis
- ☐ Loose Joint Bodies
- ☐ Deviation in Form

##### B) Fossa/Eminence

- ☐ Flattening
- ☐ Subcortical Sclerosis
- ☐ Surface Erosion

##### C) Diagnosis

- ☐ Normal
- ☐ Indeterminant
- ☐ Osteoarthritis
- ☐ Other (List):

##### D) Miscellaneous

- ☐ Ankylosis

#### I. TMJ Finding(s)

##### A. Right TMJ

PanRtIA1	
PanRtIA2	
PanRtIA3	
PanRtIA4	
PanRtIA5	
PanRtIA6	
PanRtIA7	
PanRtIA8	
PanRtIA9	
PanRtIA10	

0 - No  
1 - Yes  
9 - missing

Gross Hypoplasia  
Gross Hyperplasia  
Flattening  
Subcortical Sclerosis  
Subcortical Cyst  
Surface Erosion  
Osteophyte  
Generalized Sclerosis  
Loose Joint Bodies  
Deviation in Form

That these variables are about the  
condylar head of the TMJ is 'lost in  
translation'!

## ‘meaning’ of values in data collections

I. TMJ Finding(s)		0 - No 1 - Yes 9 - missing
A.	Right TMJ	
PanRtIA1		Gross Hypoplasia
PanRtIA2		Gross Hyperplasia
PanRtIA3		Flattening
PanRtIA4		Subcortical Sclerosis
PanRtIA5		Subcortical Cyst
PanRtIA6		Surface Erosion
PanRtIA7		Osteophyte
PanRtIA8		Generalized Sclerosis
PanRtIA9		Loose Joint Bodies
PanRtIA10		Deviation in Form

*‘The patient with patient identifier ‘PtID4’ is stated to have had a panoramic X-ray of the mouth which is interpreted to show subcortical sclerosis of that patient’s condylar head of the right temporomandibular joint’*

The screenshot shows an Excel spreadsheet with the following data:

	A	B	C	D	E	F	G	H	I	J	K	
1	PtID	PanRtIA1	PanRtIA2	PanRtIA3	PanRtIA4	PanRtIA5	PanRtIA6	PanRtIA7	PanRtIA8	PanRtIA9	PanRtIA10	...
2	PtID1	0	0	0	1	9	0	0	0	0	0	
3	PtID2	0	1	0	1	0	0	0	0	0	0	
4	PtID3	0	0	0	9	0	0	0	0	0	0	
5	PtID4	0	0	0	1	1	0	9	0	1	1	
6	PtID5	0	1	9	1	0	0	0	1	0	0	
7	PtID6	0	0	0	1	2	0	0	0	0	0	
8	PtID7	0	0	0	1	0	0	0	0	0	0	
9	...											

A red arrow points from the word "meaning" to the value "1" in cell E5.



## Objectives of the ‘sources’ analysis

- Find for each value  $V$  in the data collections all possible configurations of entities (according to our best scientific understanding) for which the following can be true:
  - $V$
  - ‘it is stated that  $V$ ’
- Describe these possible configurations by means of sentences from a formal language that mimic the structure of reality.



## Objectives of the ‘sources’ analysis (2)

- For example,
  - for the value stating that *‘The patient with patient identifier ‘PtID4’ has had a panoramic X-ray of the mouth which is interpreted to show subcortical sclerosis of that patient’s condylar head of the right temporomandibular joint’* to be true,
  - this statement must have been made,
  - for the statement to be true, there must have been that patient, an X-ray, etc, ...
  - BUT! It is not necessarily true that that patient has indeed the sclerosis as diagnosed.

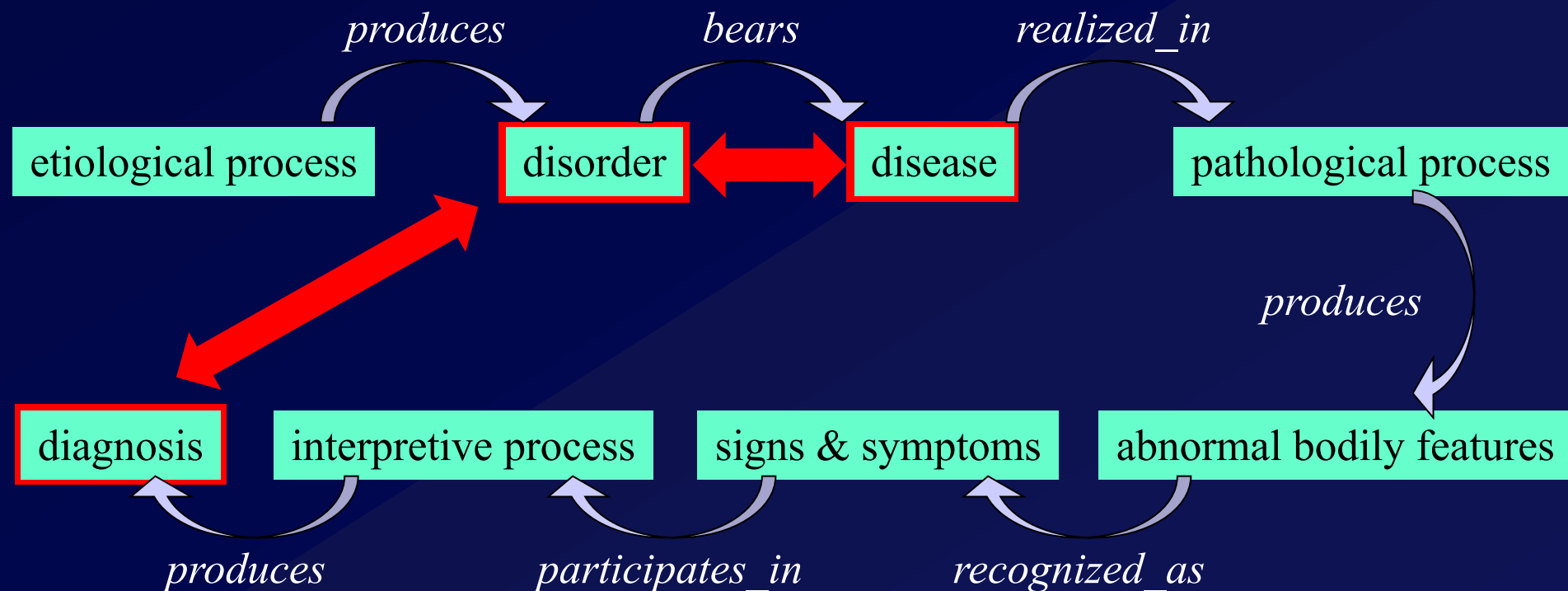




## Methodology

1. Formulate for each variable in the data collection a sentence explaining as accurately as possible what the variable stands for,
2. list the entities in reality that the terms in the sentence denote,
3. list recursively for all entities listed further entities that ontologically must exist for the entity under scrutiny to exist,
4. classify all entities in terms of realism-based ontologies (RBO),
5. specify all obtaining relationships between these entities,
6. outline all possible configurations of such entities for the sentence to be true.

## RBO (1): Ontology of General Medical Science

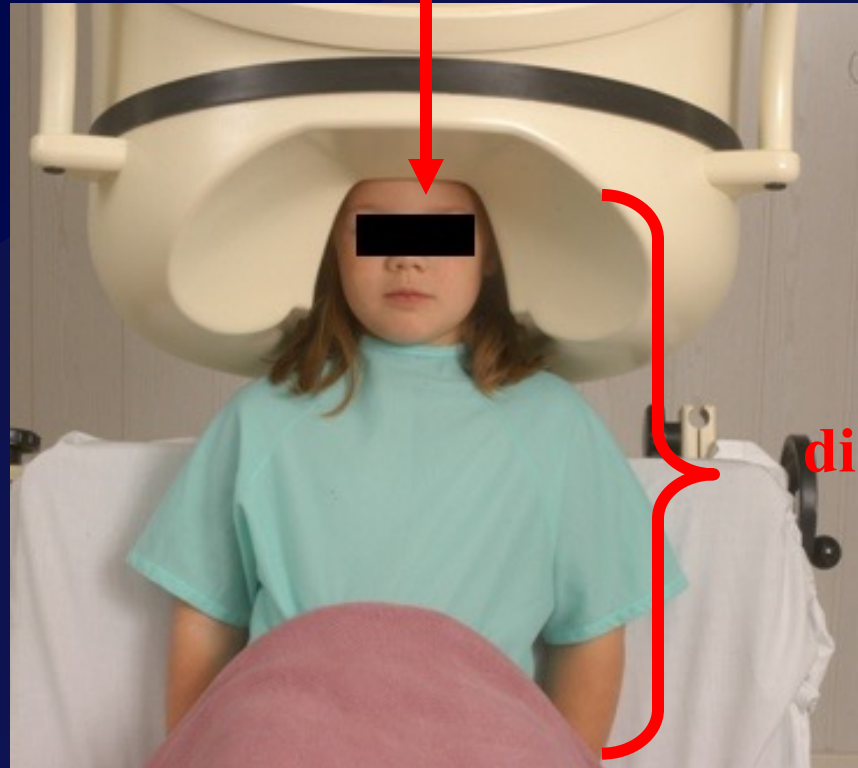


## No conflation of diagnosis, disease, and disorder

The diagnosis is here



The disorder is there



The  
disease is  
there



## OGMS: Disorder

- **Disorder** =def. – A causally linked combination of physical components that is
  - (a) clinically abnormal and
  - (b) maximal, in the sense that it is not a part of some larger such combination.
- - something is clinically abnormal if:
  - (1) is not part of the life plan for an organism of the relevant type (unlike aging or pregnancy),
  - (2) is causally linked to an elevated risk either of pain or other feelings of illness, or of death or dysfunction, and
  - (3) is such that the elevated risk exceeds a certain threshold level.

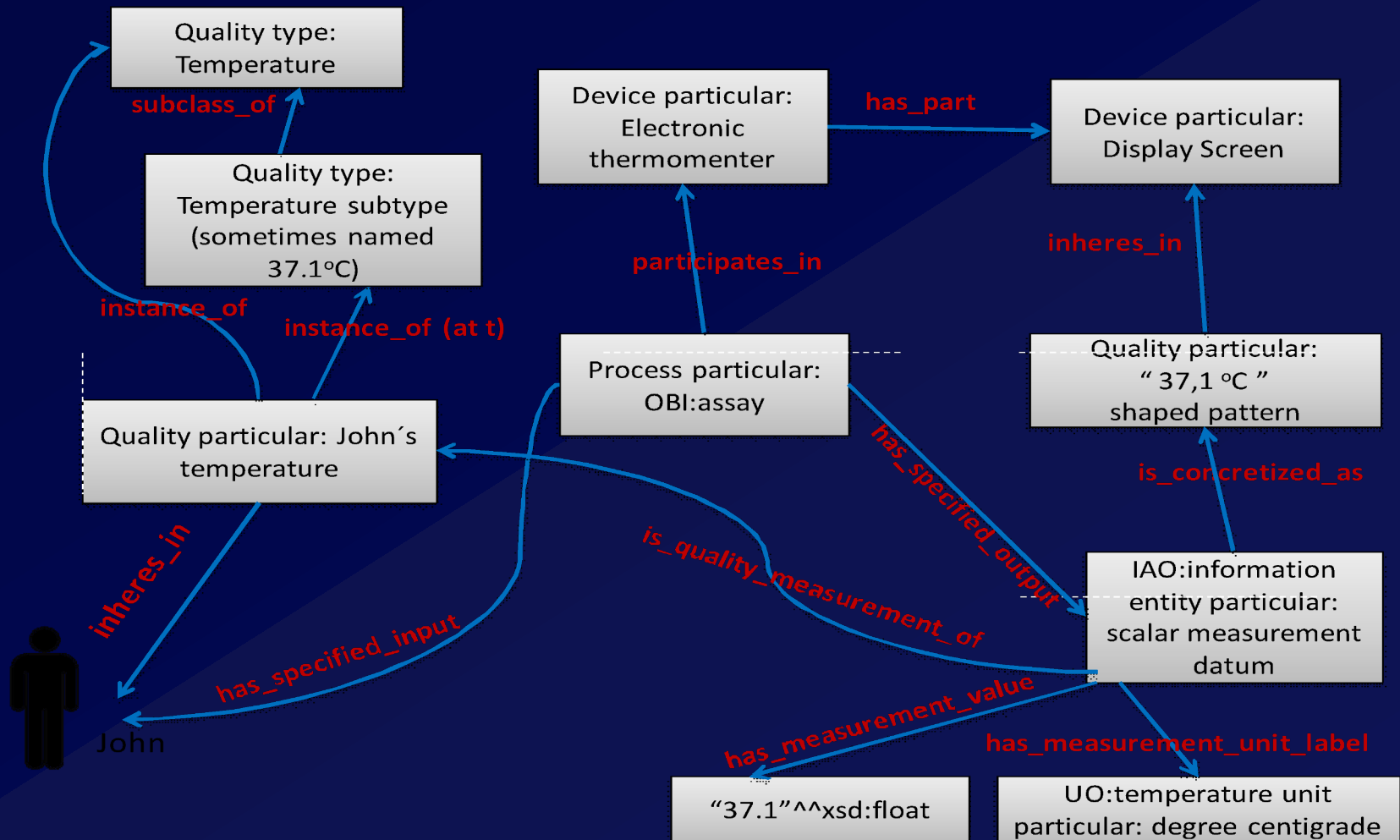


## OGMS: Diagnosis

- **Clinical Picture** =def. – A representation of a clinical phenotype that is inferred from the combination of laboratory, image and clinical findings about a given patient.
- **Diagnosis** =def. –
  - A conclusion of an interpretive process that has as input a clinical picture of a given patient and as output an assertion to the effect that the patient has a disease of such and such a type.



## RBO (2): (cleaned up) Ontology of Biomedical Investigations



## Step 1: formulate a statement

I. TMJ Finding(s)		0 - No 1 - Yes 9 - missing
A.	Right TMJ	
PanRtIA1		Gross Hypoplasia
PanRtIA2		Gross Hyperplasia
PanRtIA3		Flattening
PanRtIA4		Subcortical Sclerosis
PanRtIA5		Subcortical Cyst
PanRtIA6		Surface Erosion
PanRtIA7		Osteophyte
PanRtIA8		Generalized Sclerosis
PanRtIA9		Loose Joint Bodies
PanRtIA10		Deviation in Form

*‘The patient with patient identifier ‘PtID4’ is stated to have had a panoramic X-ray of the mouth which is interpreted to show subcortical sclerosis of that patient’s condylar head of the right temporomandibular joint’*

The screenshot shows an Excel spreadsheet with the following data:

	A	B	C	D	E	F	G	H	I	J	K	
1	PtID	PanRtIA1	PanRtIA2	PanRtIA3	PanRtIA4	PanRtIA5	PanRtIA6	PanRtIA7	PanRtIA8	PanRtIA9	PanRtIA10	...
2	PtID1	0	0	0	1	9	0	0	0	0	0	
3	PtID2	0	1	0	1	0	0	0	0	0	0	
4	PtID3	0	0	0	9	0	0	0	0	0	0	
5	PtID4	0	0	0	1	1	0	9	0	1	1	
6	PtID5	0	1	9	1	0	0	0	1	0	0	
7	PtID6	0	0	0	1	2	0	0	0	0	0	
8	PtID7	0	0	0	1	0	0	0	0	0	0	
9	...											

A red arrow points from the word "meaning" to the value "1" in cell E5.

## Step 2 (1): list the entities denoted

- 1(*The patient*) with  
2(*patient identifier 'PtID4'*)  
3(*is stated*) 4(*have had*) a  
5(*panoramic X-ray*) of  
6(*the mouth*) which 7(*is*  
*interpreted*) to 8(*show*)  
9(*subcortical sclerosis of*  
10(*that patient's condylar*  
*head of the* 11(*right*  
*temporomandibular*  
*joint*)))'

	CLASS	INSTANCE IDENTIFIER
	person	IUI-1
	patient identifier	IUI-2
	assertion	IUI-3
	technically investigating	IUI-4
	panoramic X-ray	IUI-5
	mouth	IUI-6
	interpreting	IUI-7
	seeing	IUI-8
	diagnosis	IUI-9
	condylar head of right TMJ	IUI-10
	right TMJ	IUI-11

notes:

colors have no meaning here, just provide easy reference,  
this first list can be different, any such differences being resolved in step 3



## Step 2 (2): provide *directly referential* descriptions

CLASS	INSTANCE IDENTIFIER	DIRECTLY REFERENTIAL DESCRIPTIONS
person	IUI-1	the person to whom IUI-2 is assigned
patient identifier	IUI-2	the patient identifier of IUI-1
assertion	IUI-3	'the patient with patient identifier PtID4 has had a panoramic X-ray of the mouth which is interpreted to show subcortical sclerosis of that patient's right temporomandibular joint'
technically investigating	IUI-4	the technically investigating of IUI-6
panoramic X-ray	IUI-5	the panoramic X-ray that resulted from IUI-4
mouth	IUI-6	the mouth of IUI-1
interpreting	IUI-7	the interpreting of the signs exhibited by IUI-5
seeing	IUI-8	the seeing of IUI-5 which led to IUI-7
diagnosis	IUI-9	the diagnosis expressed by means of IUI-3
condylar head of right TMJ	IUI-10	the condylar head of the right TMJ of IUI-1
right TMJ	IUI-11	the right TMJ of IUI-1



## Step 3: identify further entities that ontologically must exist for each entity under scrutiny to exist.

assigner role	IUI-12	the assigner role played by the entity while it performed IUI-21
assigning	IUI-21	the assigning of IUI-2 to IUI-1 by the entity with role IUI-12
asserting	IUI-20	the asserting of IUI-3 by the entity with asserter role IUI-13
asserter role	IUI-13	the asserter role played by the entity while it performed IUI-20
investigator role	IUI-14	the investigator role played by the entity while it performed IUI-4
panoramic X-ray machine	IUI-15	the panoramic X-ray machine used for performing IUI-4
image bearer	IUI-16	the image bearer in which IUI-5 is concretized and that participated in IUI-8
interpreter role	IUI-17	the interpreter role played by the entity while it performed IUI-7
perceptor role	IUI-18	the perceptor role played by the entity while it performed IUI-8
diagnostic criteria	IUI-19	the diagnostic criteria used by the entity that performed IUI-7 to come to IUI-9
study subject role	IUI-22	the study subject role which inheres in IUI-1





## Step 3: some remarks

- interpreter role, perceptor role, ...
  - reference to roles rather than the entity in which the roles inhere because it may be the same entity and one should not assign several IUIs to the same entity
- each description follows similar principles as Aristotelian definitions but is about particulars rather than universals



## Step 4: classify all entities in terms of realism-based ontologies

CLASS	HIGHER CLASS
person	BFO: Object
patient identifier	IAO: Information Content Entity
assertion	IAO: Information Content Entity
technically	OBI: Assay
investigating	
panoramic X-ray	IAO: Image
mouth	FMA: Mouth
interpreting	MFO: Assessing
seeing	BFO: Process
diagnosis	IAO: Information Content Entity
condylar head of right TMJ	FMA: Right condylar process of mandible
right TMJ	FMA: Right temporomandibular joint
assigner role	BFO: Role
assigning	BFO: Process
study subject role	OBI: Study subject role

- requires more ontological and philosophical skills than domain expertise or expertise with Protégé,
- not just term matching



## Step 5: specify relationships between these entities

- For instance:
  - at least during the taking of the X-ray the study subject role inheres in the patient being investigated:
    - IUI-23 *inheres-in* IUI-1 *during* t1
  - the patient participates at that time in the investigation
    - IUI-4 *has-participant* IUI-1 *during* t1
- These relations need to follow the principles of the Relation Ontology.



**Step 6: outline all possible configurations of such entities for the sentence to be true** (a one semester course on its own)

- Such outlines are collections of relational expressions of the sort just described,
- Variant configurations for the example:
  - perceptor and interpreter are the same or distinct human beings,
  - the X-ray machine is unreliable and produced artifacts which the interpreter thought to be signs motivating his diagnosis, while the patient has indeed the disorder specified by the diagnosis (the clinician was lucky)
  - ...



## Conclusion

- Realism-based ontology has a lot to offer to make data collections comparable and unambiguously understandable.
- It is hard !
- How far one needs to go depends on the purposes.
  - ideally: an analysis should be such that it can accommodate ALL purposes, i.e. the analysis should be independent of any purpose;
    - distinction between reference ontologies and application ontologies.