PSIP

A European Project on Patient Safety

www.psip-project.eu

Patient Safety through Intelligent Procedures in medication

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And the PSIP Consortium

2007 - 2013

PROJECT PARTNERS

1. University Hospital of Lille and University of Lille2 (F)
2. University Hospital of Rouen (F)
3. Denain General Hospital (F)
4. 10 hospitals from the « Capital Region of Copenhagen » (DK)

5. Oracle (Europe)
6. IBM Denmark – division ACURE (DK)
7. Medasys (F)
8. Vidal SA (F)
9. KITE solutions (I)
10. Ideea Advertising (Romania)

11. Aristotle Thessaloniki University (Greece)
12. Aalborg University (DK)
13. UMIT –Innsbruck University (A)

Scientific goals

– **Identification** of ADEs

- « To get a better knowledge of the prevalence of Adverse Drug Events (ADEs) and of their characteristics per Hospital, per Region, per Country »

– **Prevention** of ADEs

- « To develop concepts and methods to achieve the contextualization of CDSS (alerting) functions »

Scientific goals

- **Identification** of ADEs

First Question: **"Is it possible to detect and identify Adverse Drug Events by mining medical databases ?"**

- **Prevention** of ADEs

Second Question: **"Is it possible to prevent these Adverse drug Events through IT methods ?"**

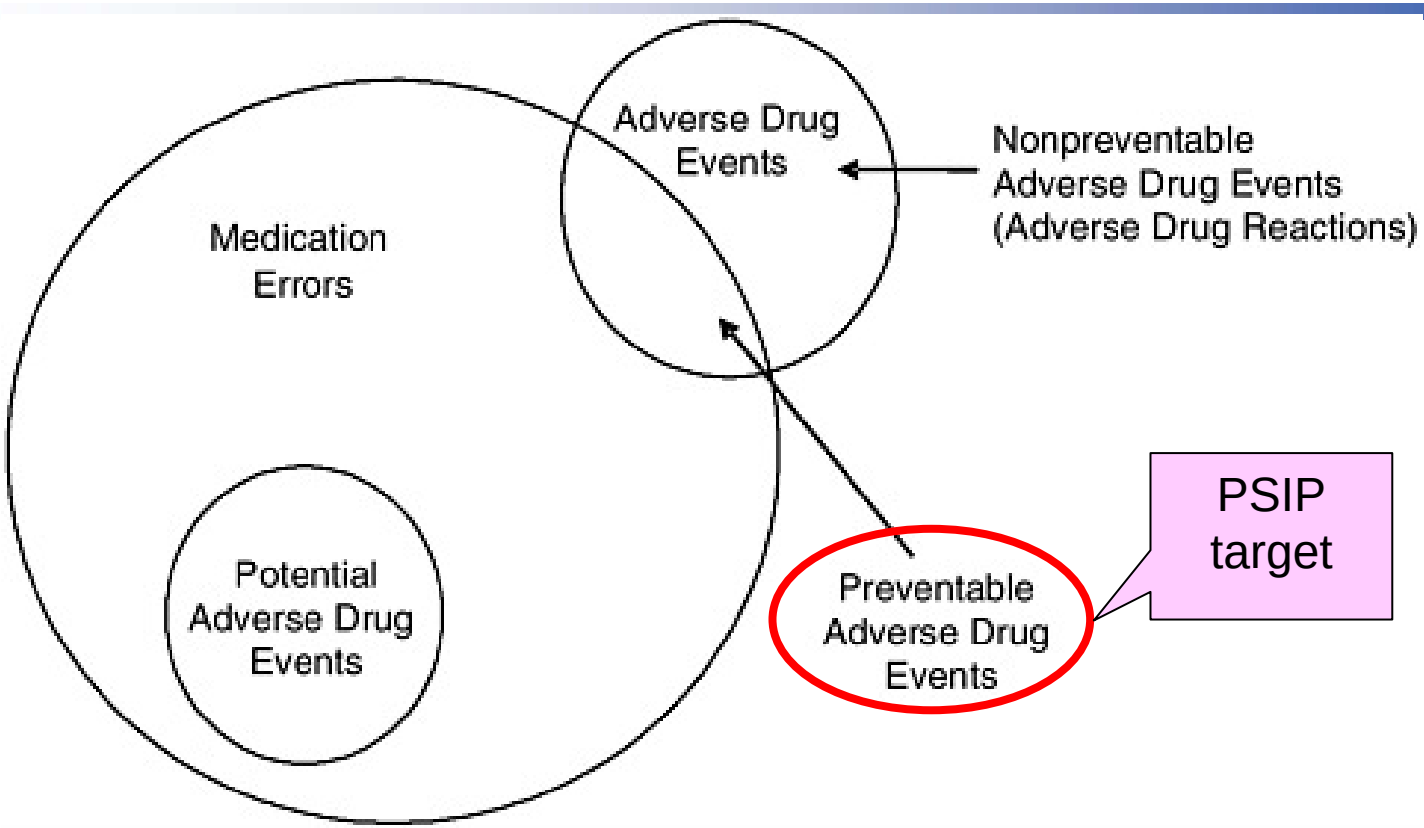
Scope of PSIP

Adverse Drug Events

- "Any **injury** occurring during the **patient's drug therapy** and resulting either from appropriate care, or from unsuitable or suboptimal care"*

- *Committee of Experts on Management of Safety and Quality in Health Care (SP-SQS) / Expert Group on Safe Medication Practices: Glossary of terms related to patient and medication safety. (http://www.who.int/patientsafety/highlights/COE_patient_and_medication_safety_gl.pdf)

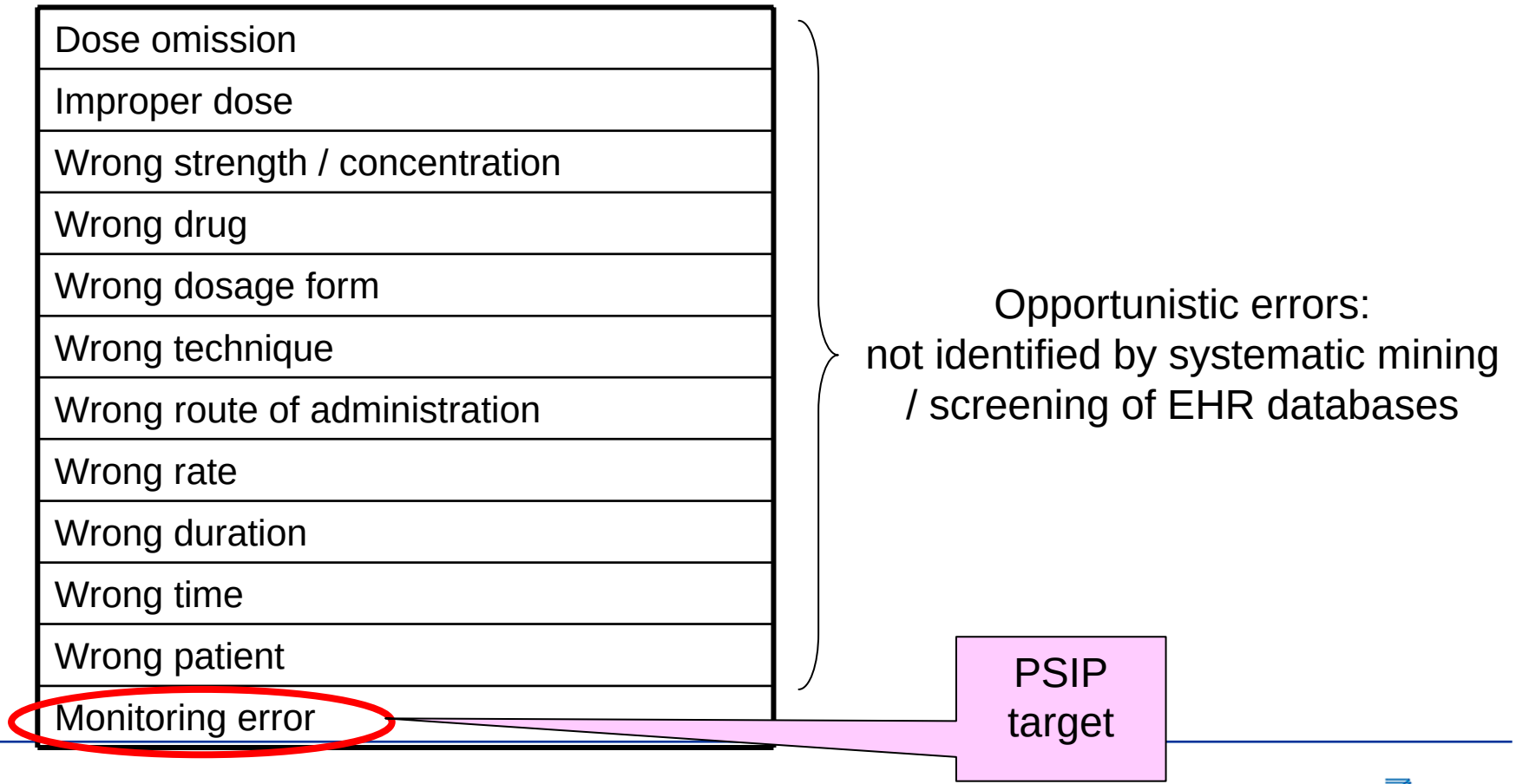
ADEs / ADRs / medication errors



Gandhi TK, Seger DL, Bates DW. 2000. Identifying drug safety issues: From research to practice. /International Journal for Quality in Health Care/ 12(1):69–76.

Taxonomy of medication errors

- NCCMERP:



Medication monitoring errors

- NCCMERP taxonomy:

Drug-drug interaction
Drug-food / nutrient interaction
Drug - documented allergy interaction
Drug-disease interaction
Deteriorated drug (out of PSIP scope)
Other

- Adapted PSIP taxonomy

Drug-drug interaction
Drug-food / nutrient interaction
Drug-documented allergy interaction
Drug-disease interaction
Drug-patient's characteristics interaction
Drug-lab value monitoring

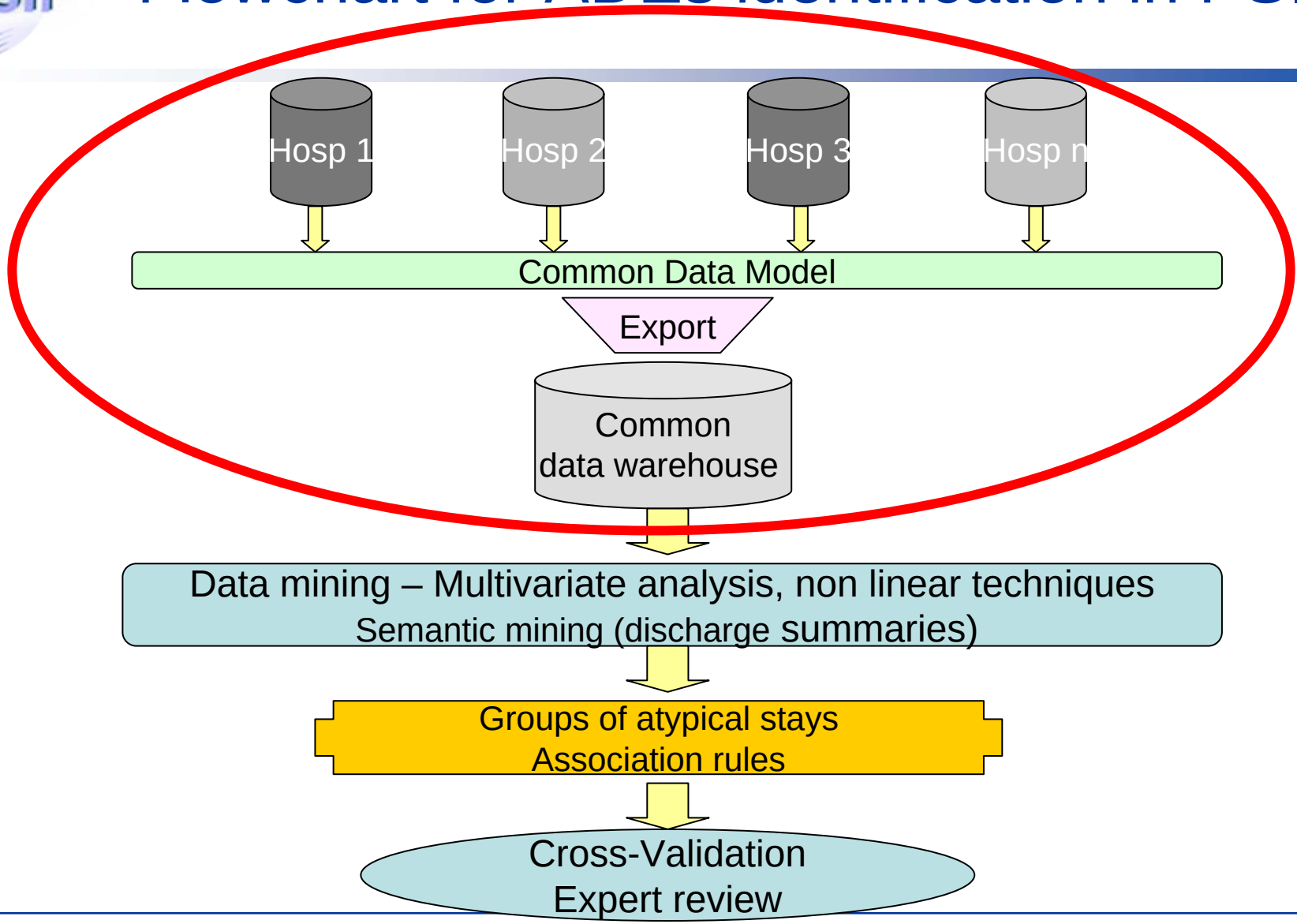
Identification of ADEs

– **Identification** of ADEs

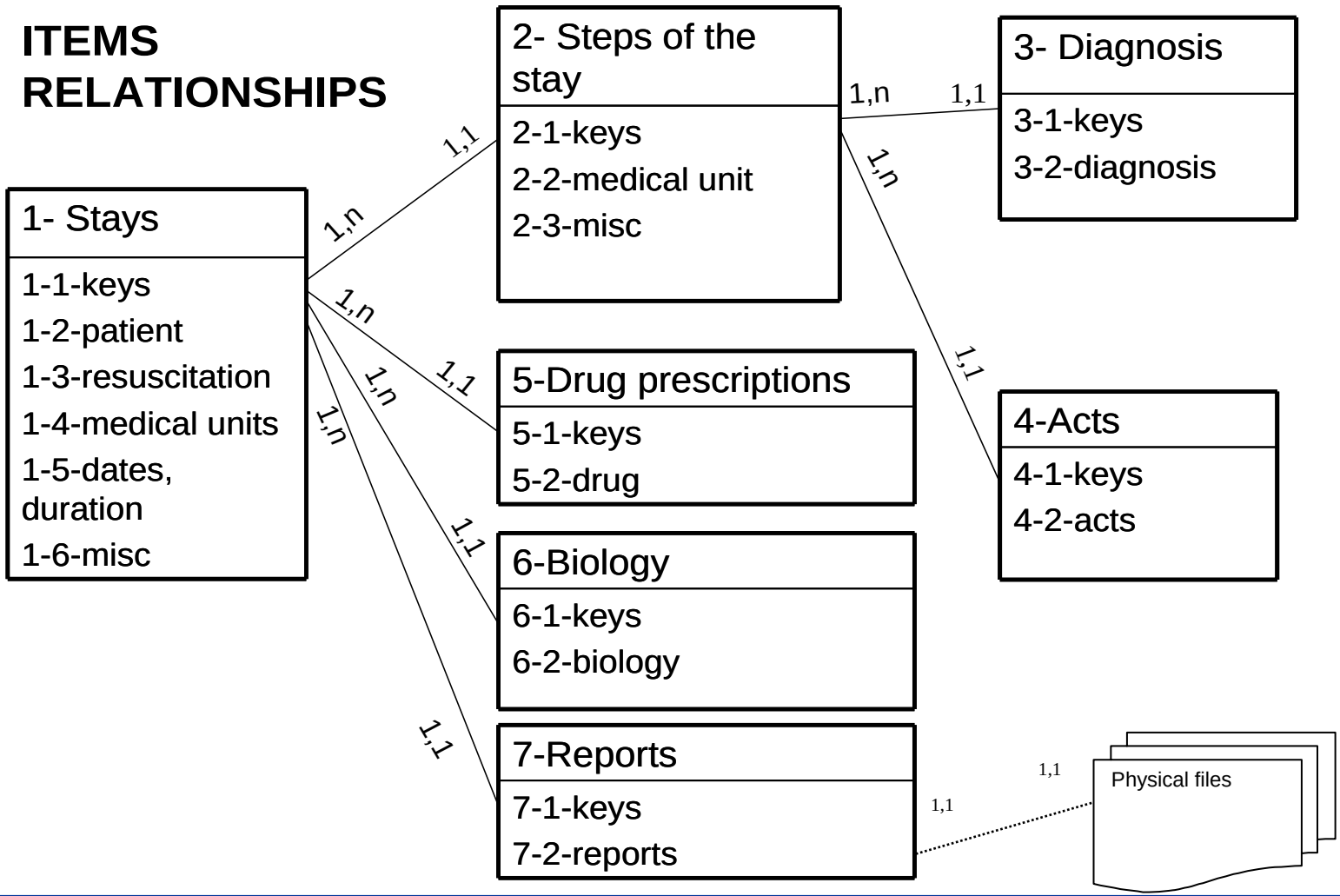
First Question: **“Is it possible to detect and identify Adverse Drug Events by mining medical databases ?”**

Step1: Obtaining Data

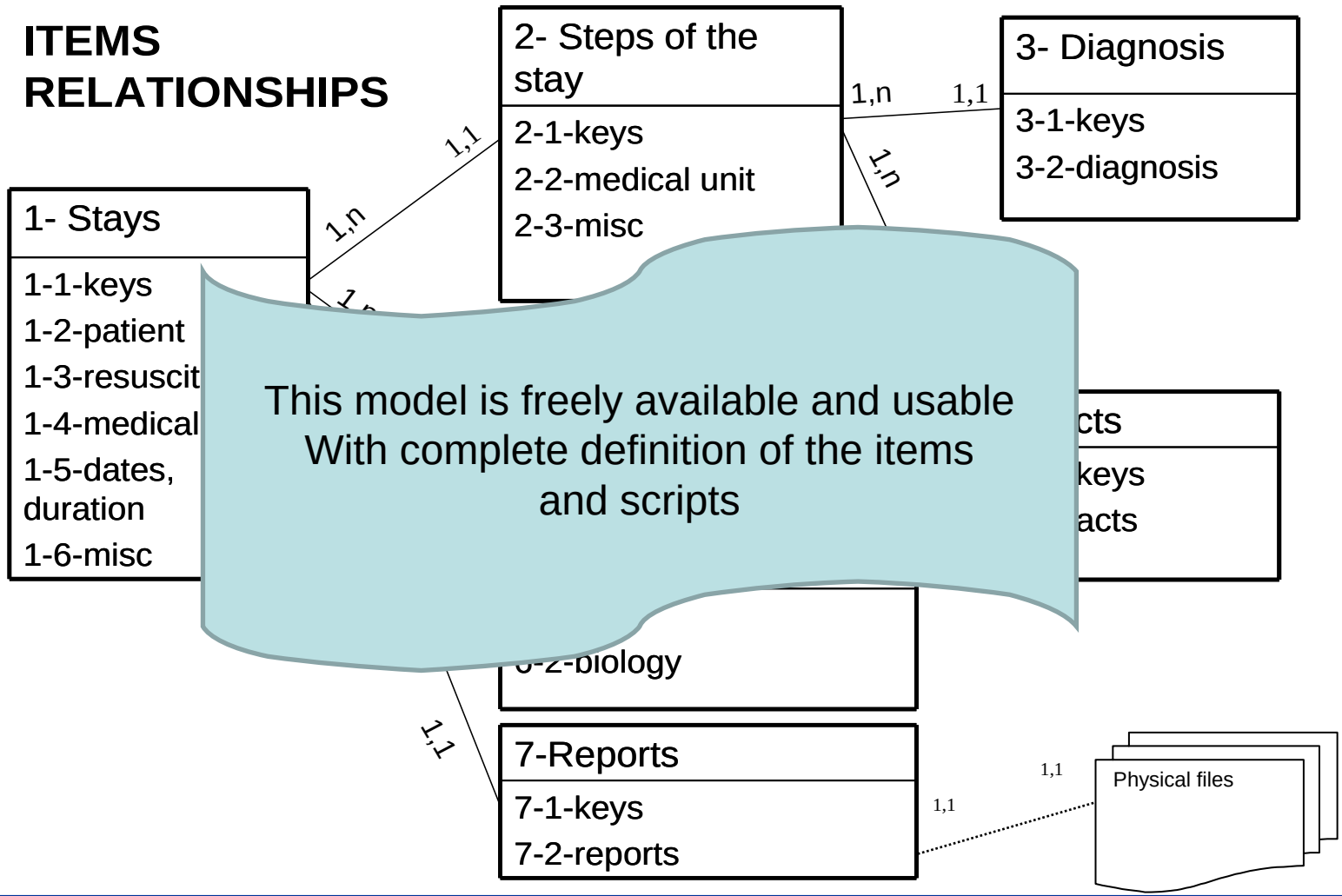
Flowchart for ADEs identification in PSIP



Common Data Model

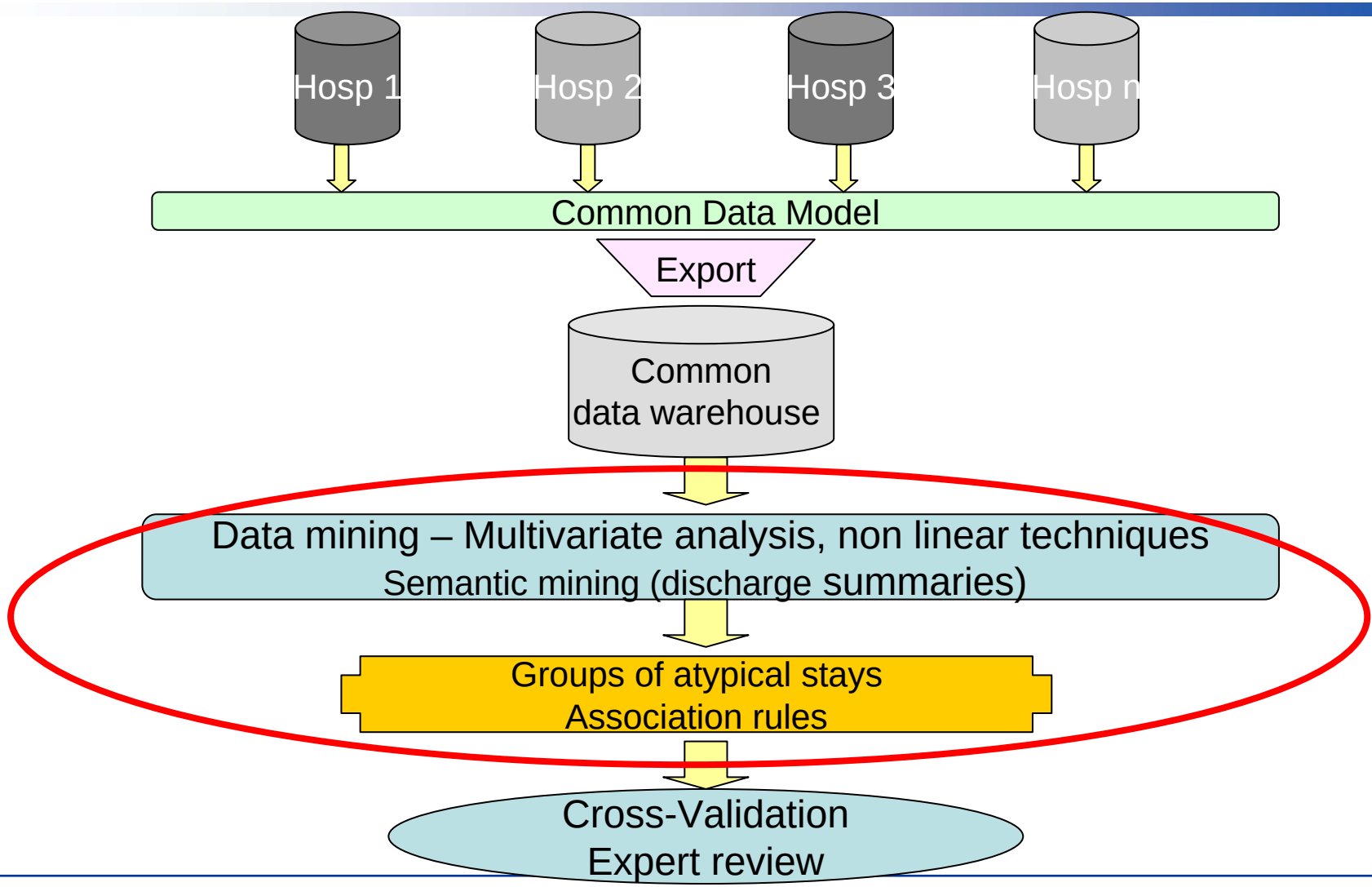


Common Data Model



Step 2: Data Mining

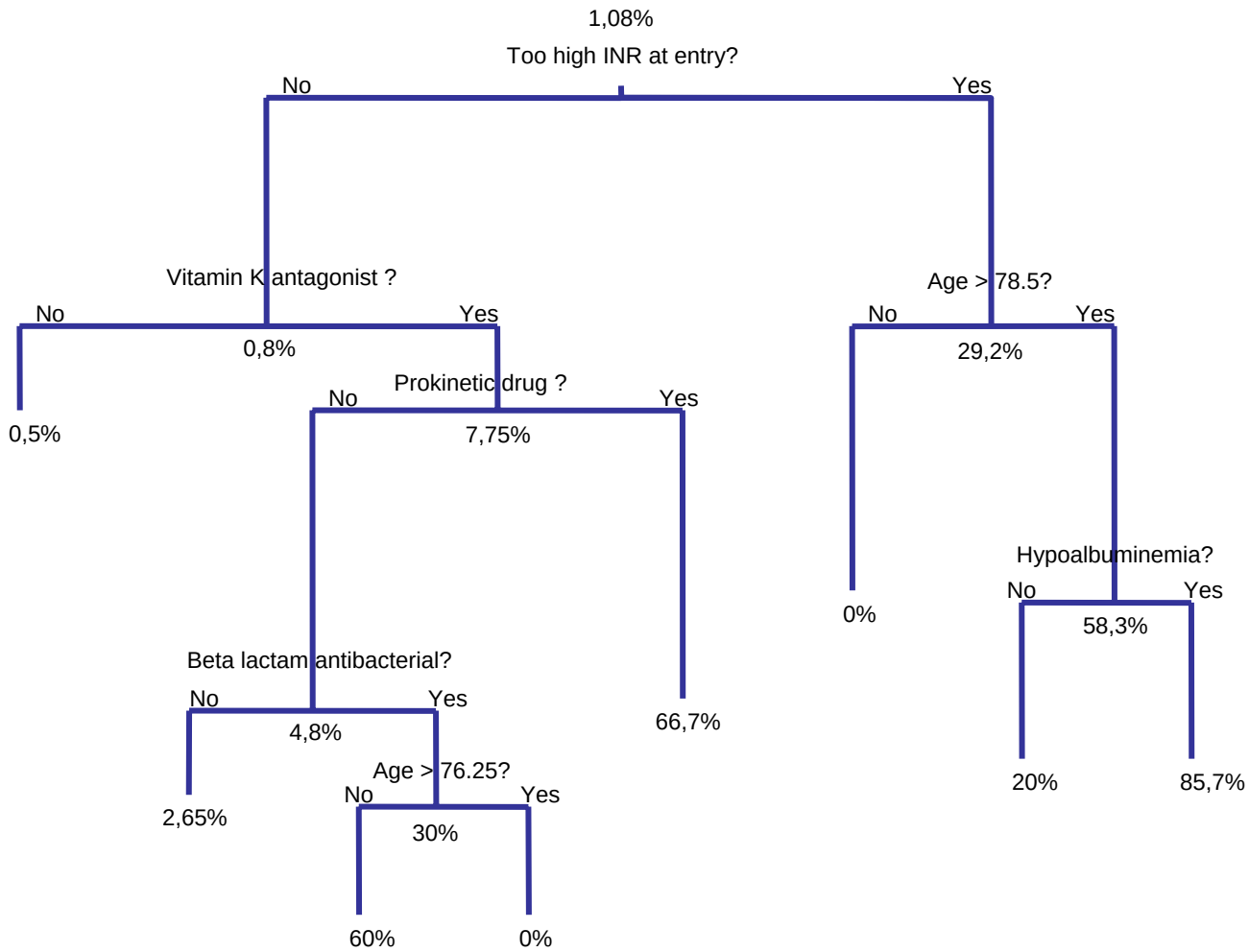
Data Mining


Hosp 1
Hosp 2
Hosp 3
Hosp n
Common Data Model
Export
Common
data warehouse
Data mining – Multivariate analysis, non linear techniques
Semantic mining (discharge summaries)
Groups of atypical stays
Association rules
Cross-Validation
Expert review

Data Mining Methods

- Multiple Correspondence analysis:
  - identification of risk factors, groups of patients at risk.
  - Some Rules, but too general, not as precise as expected
- Decision Trees (CART)
  - Efficient when applied in a coherent context (one medical department in one hospital)
  - Calculation of confidence and support
  - Identification of cases; definition of rules through the exploitation of the decision trees
- Association Rules:
  - Some improvement. New rules implemented.

Appearance of a too low INR (INR < 2) in patients undergoing anticoagulation



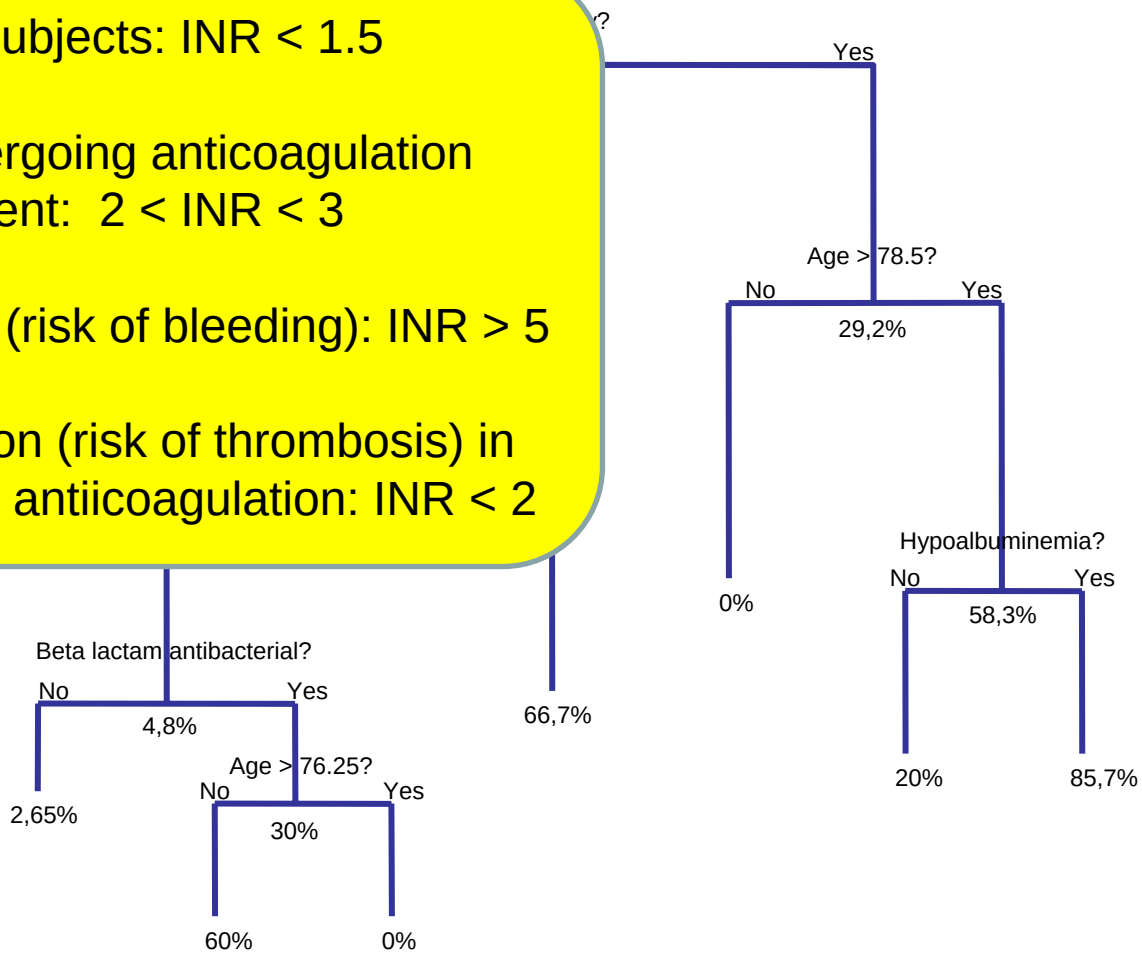
Appearance of a too low INR (INR < 2) in patients undergoing anticoagulation

Normal Subjects: INR < 1.5

Patients undergoing anticoagulation
Treatment: 2 < INR < 3

Hypocoagulation (risk of bleeding): INR > 5

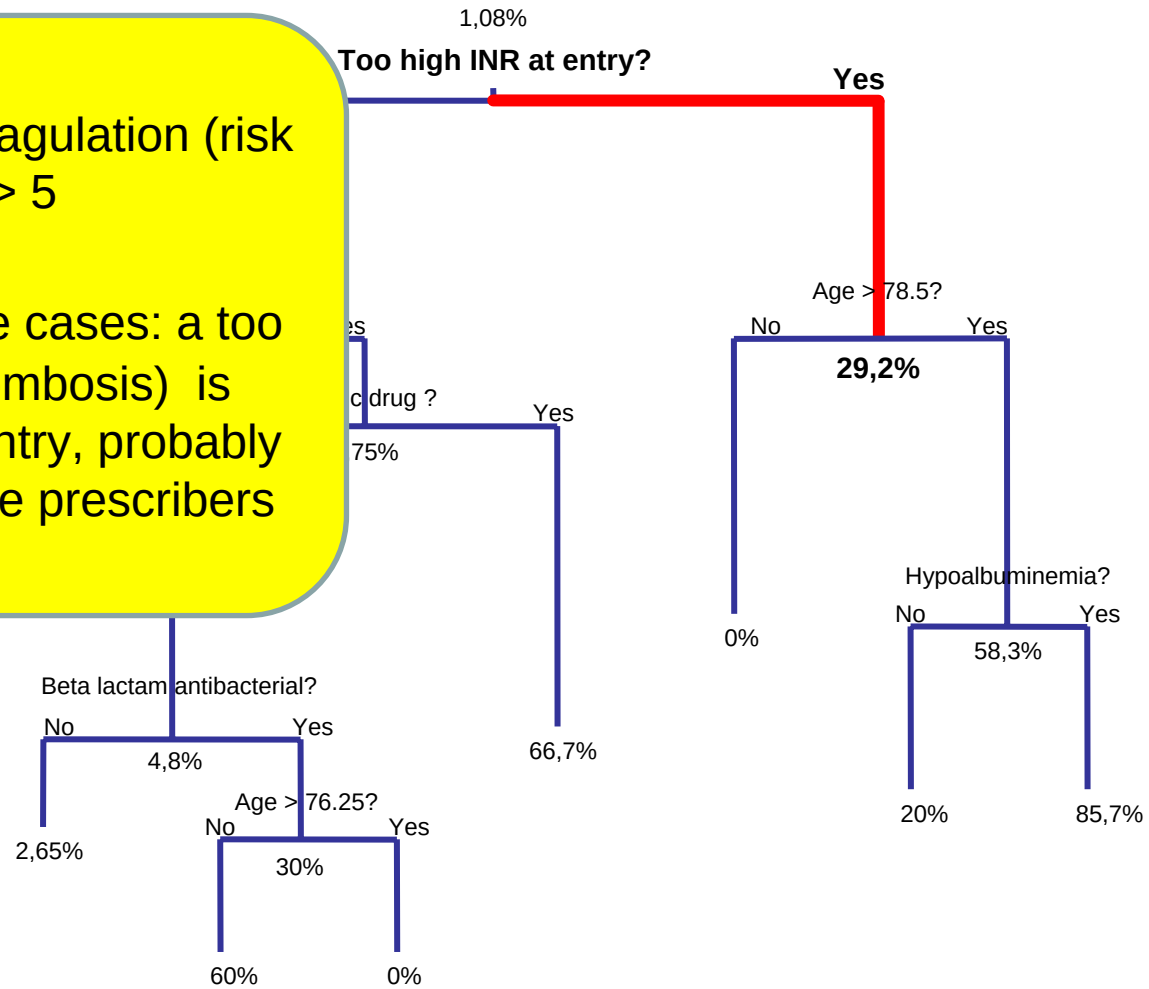
Hypercoagulation (risk of thrombosis) in patients needing antiicoagulation: INR < 2



Appearance of a too low INR (risk of thrombosis) Rule N° 1

Too high INR means Hypocoagulation (risk of bleeding): INR > 5

Interpretation: in **30%** of the cases: a too low INR (with a risk of thrombosis) is following a too high INR at entry, probably due to an over-reaction of the prescribers



Outcomes:
0% death
avg duration: 6.4 days

Appearance of a too low INR (risk of thrombosis) Rule N° 2

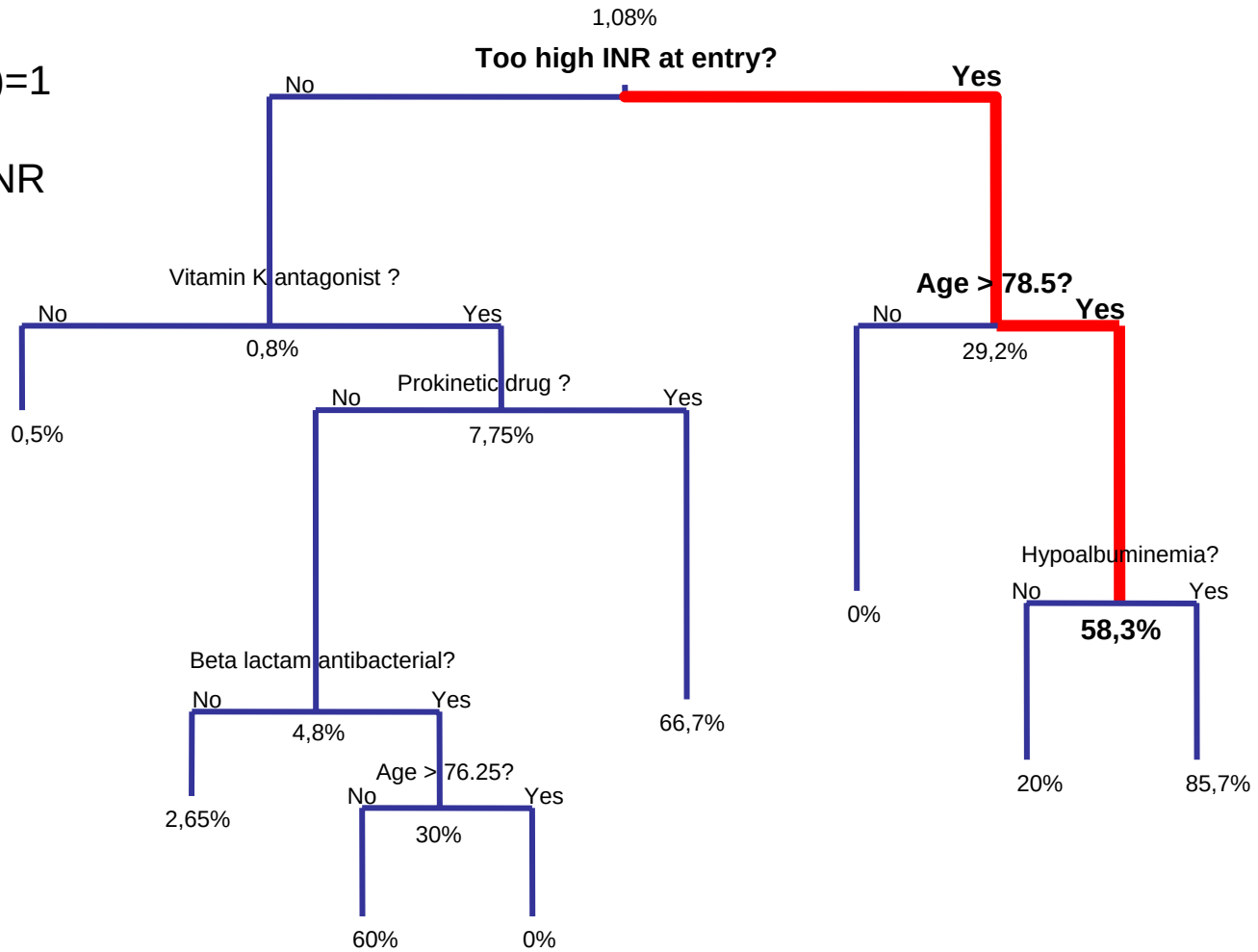
Rule enunciation:

Bio(previous too high INR)=1
& MedInfo(age)>78.68
Appearance of a too low INR

Rule characteristics:
Support: 7
Confidence: 58%

12 stays match the conditions, 7 of them present the effect (58%=7/12)

Outcomes:
0% death
avg duration: 9.3 days

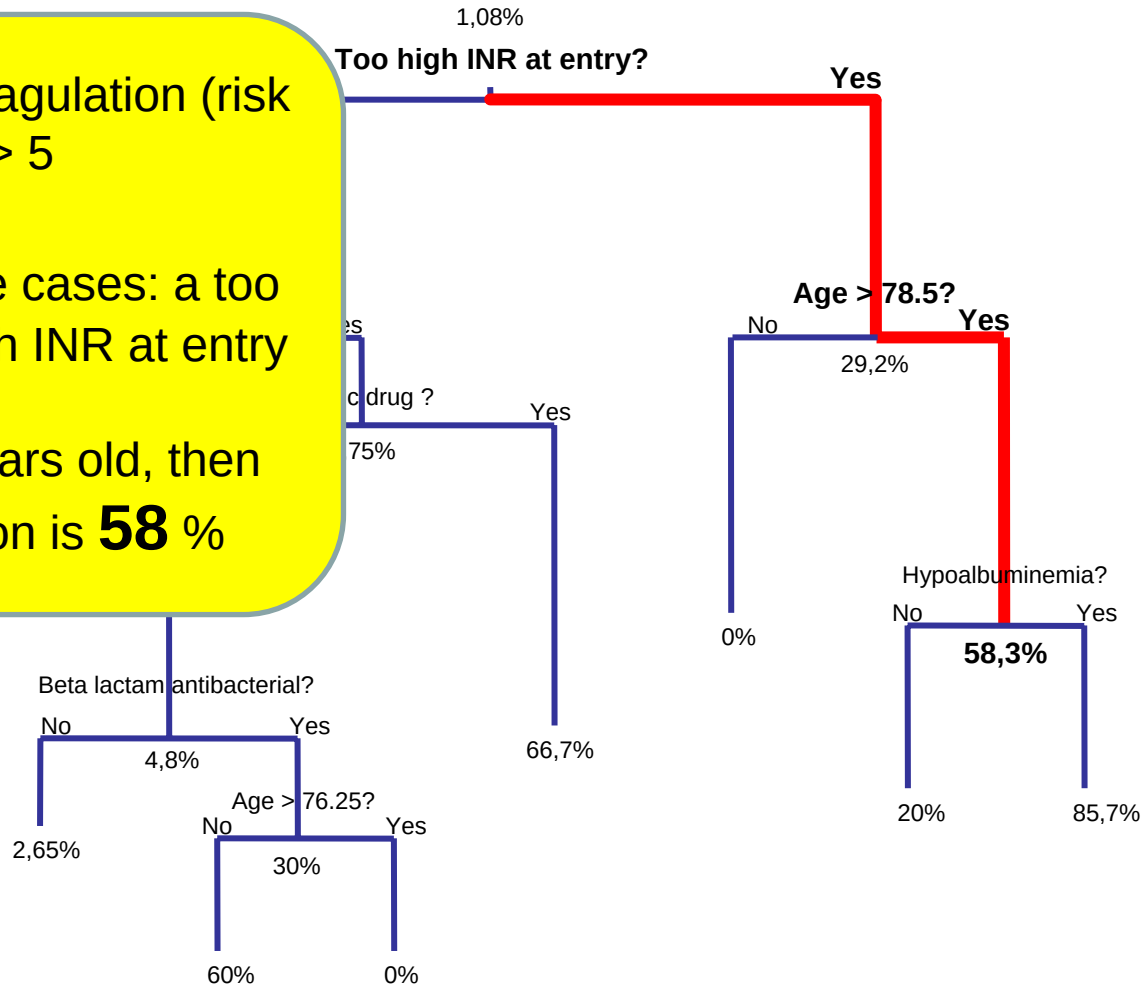


Appearance of a too low INR (risk of thrombosis) Rule N° 2

Too high INR means Hypocoagulation (risk of bleeding): INR > 5

Interpretation: in **30%** of the cases: a too low INR is following a too high INR at entry

If patient is more than 78 years old, then the risk of Hypercoagulation is **58** %



Outcomes:
0% death
avg duration: 9.3 days

Appearance of a too low INR (risk of thrombosis) Rule N° 3

Rule enunciation:

Bio(previous too high INR)=1
& MedInfo(age)>78.68
& Bio(previous hypoalbuminemia)=1
Appearance of a too low INR

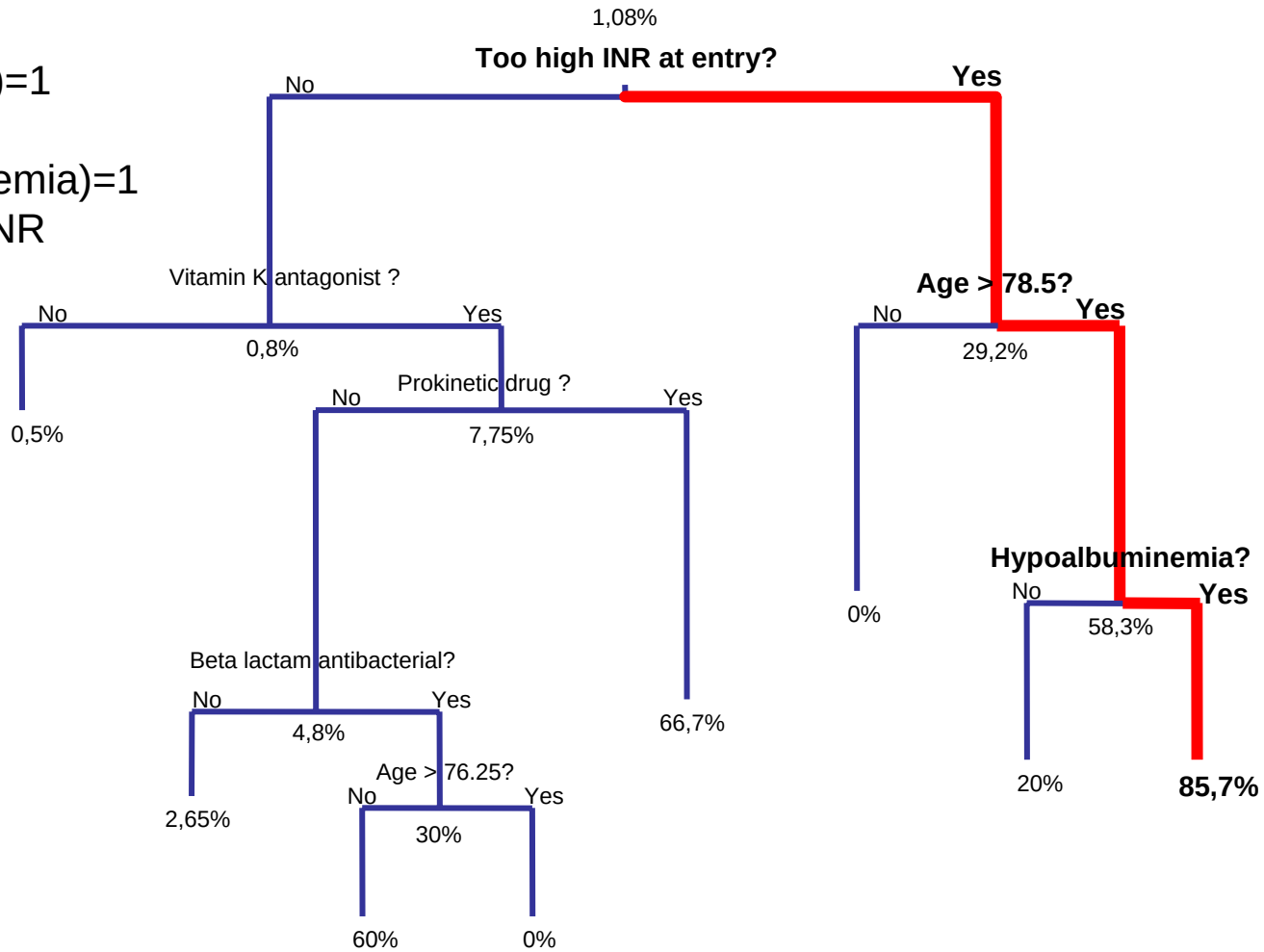
Rule characteristics:

Support: 6
Confidence: 86%

7 stays match the conditions, 6 of them present the effect (86%=6/7)

Outcomes:

0% death
avg duration: 13.4 days

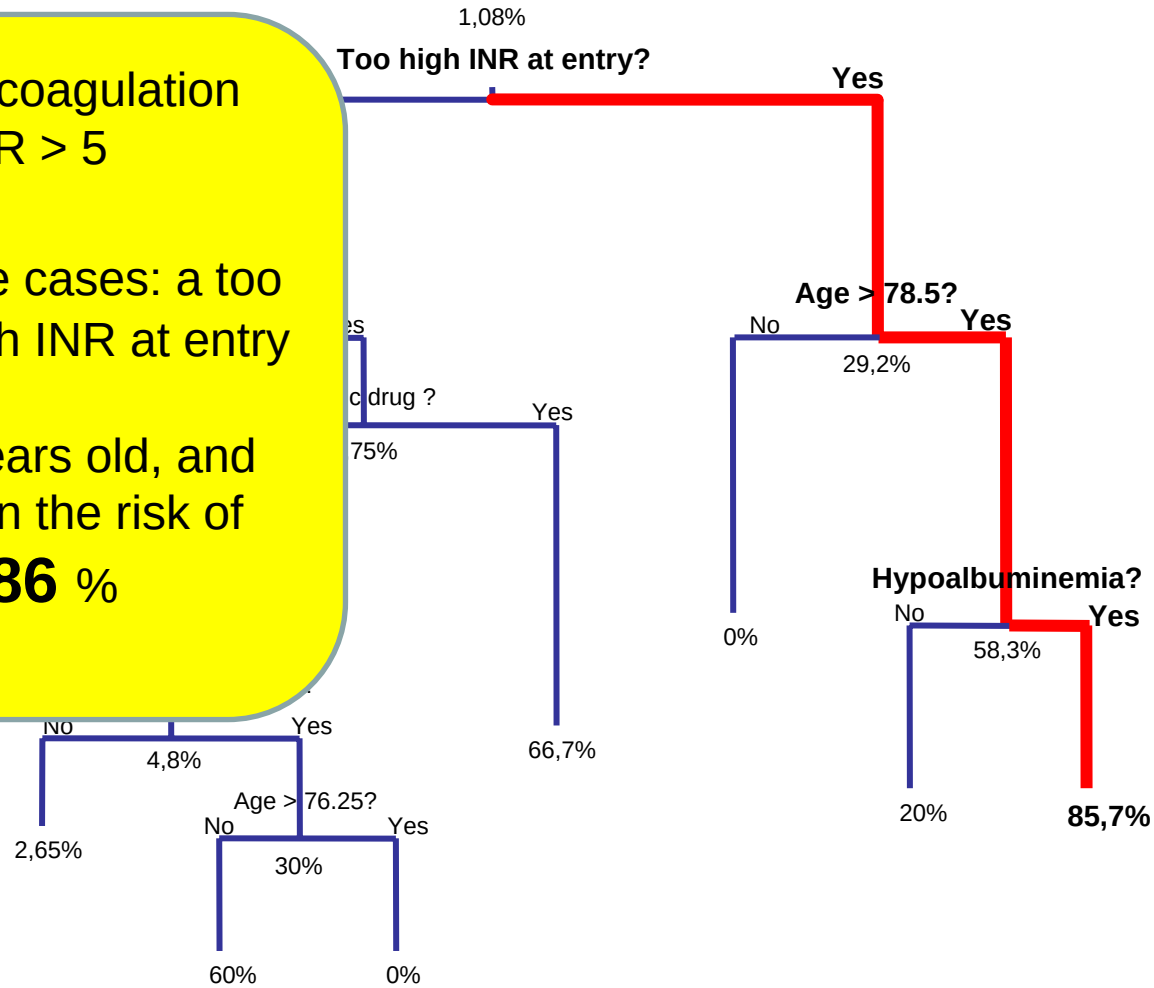


Appearance of a too low INR (risk of thrombosis) Rule N° 3

Too high INR means Hypocoagulation (risk of bleeding): INR > 5

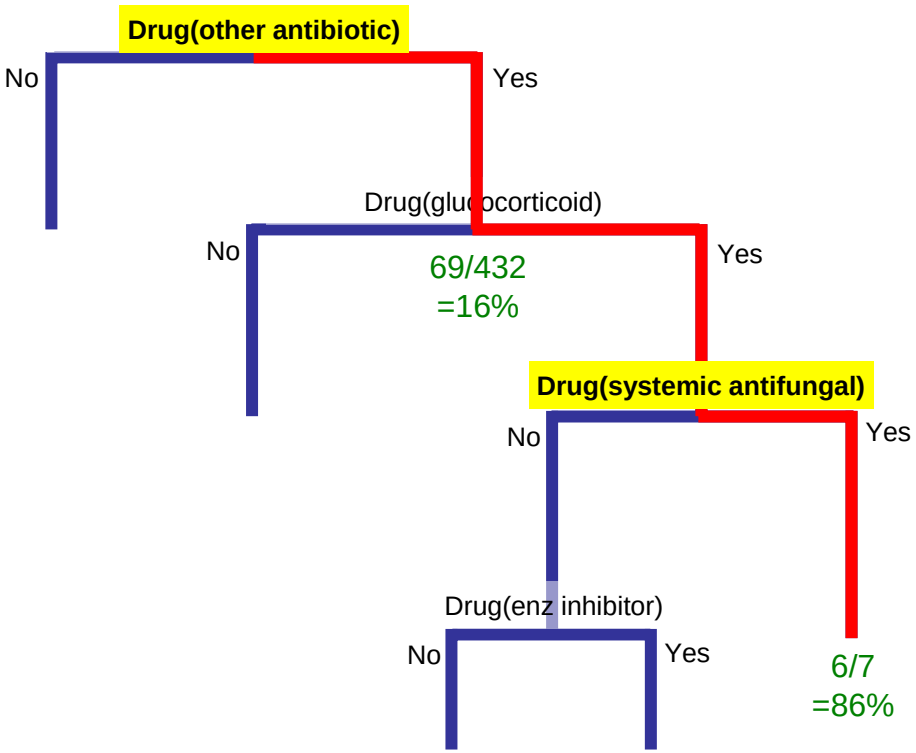
Interpretation: in **30%** of the cases: a too low INR is following a too high INR at entry

If patient is more than 78 years old, and with hypoalbuminemia, then the risk of Hypercoagulation is **86** %



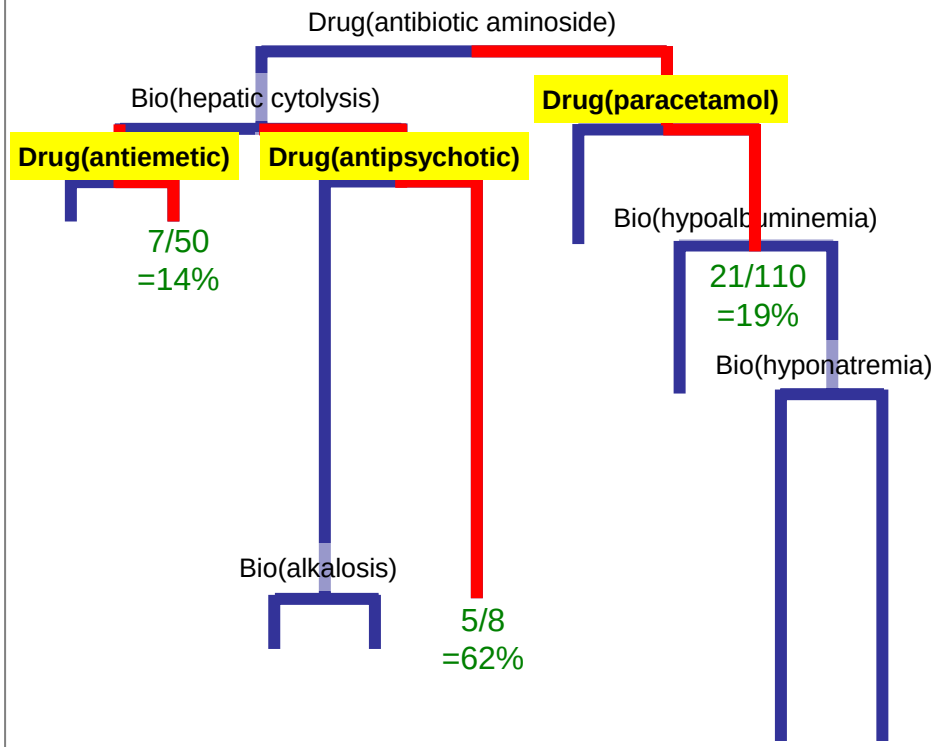
Outcomes:
0% death
avg duration: 13.4 days

Second Example: Appearance of a thrombocytopenia



Tree from Denain, Fr

(Medicine unit) : 2.08%

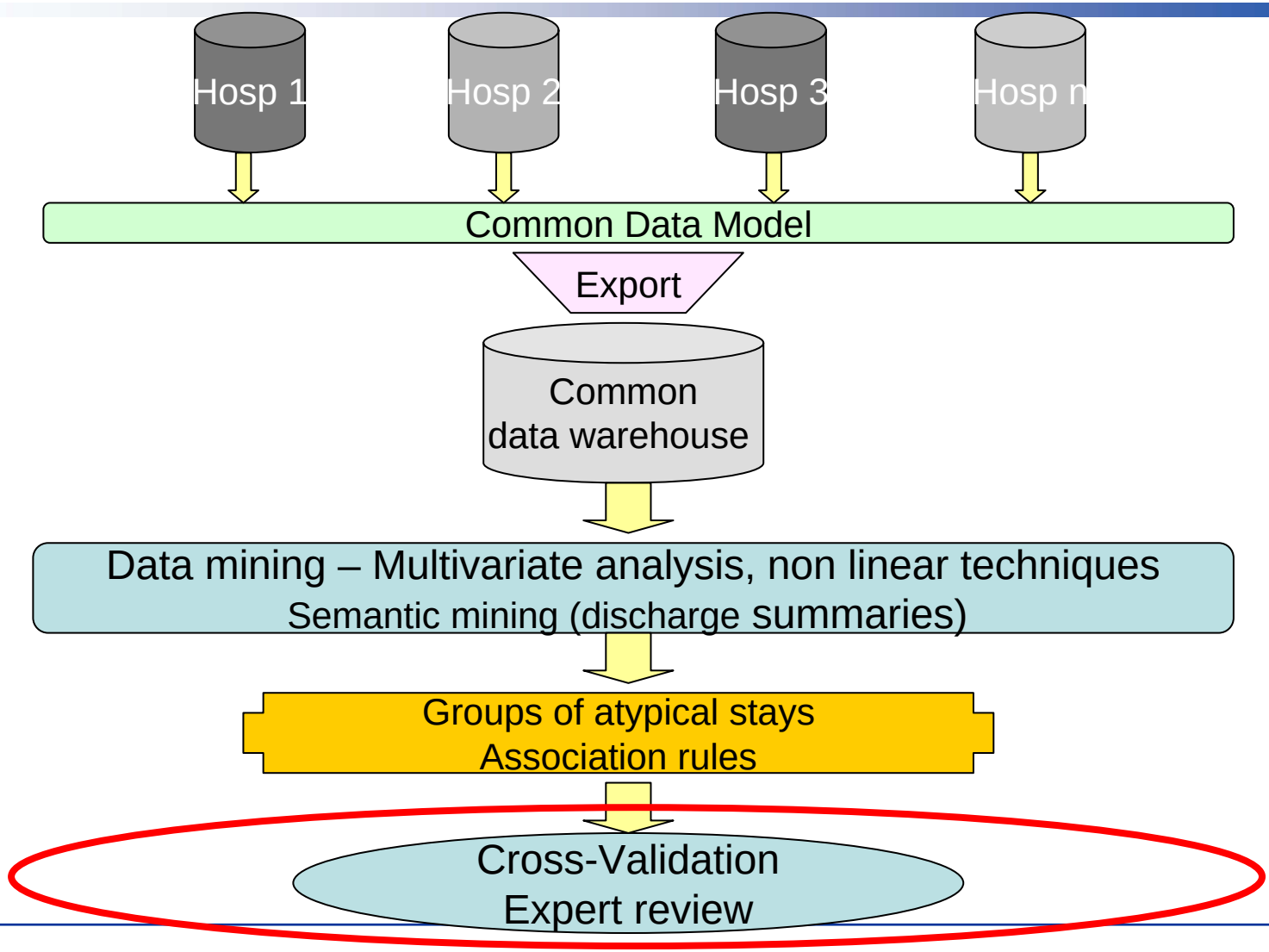


Tree from Copenhagen, Dk

(Cardiology unit): 0.37%

Step 3: Knowledge elicitation. Validation of the Knowledge Rules

Knowledge elicitation



Generation of the corresponding Rule

CONDITION	CONCLUSION	CONFIDENCE	SUPPORT
Bio (previous too high INR) = 1 & MedInfo (age)>78	**Risk of Low INR**	**56 %**	**7**

Generation of the corresponding Rule

CONDITION	CONCLUSION	CONFIDENCE	SUPPORT
Bio (previous too high INR) = 0 & Drug(vitamin K antagonist)=1 & Drug(prokinetic)=1	**Risk of Low INR**	**67%**	**4**

Rules Validation

- Currently: 600 Decision Trees
- 250 rules

- Validation of rules is mandatory:
  - Matched against existing Experts rules
  - Or verified against scientific references
  - Or validated by physio-pathologic knowledge

Validation of the association rules

- Confrontation to existing scientific knowledge retrieved from various sources:

Systematically	Pharmacorama
	Automated Data Bank onDrugs (Vidal)
	Theriaque
If necessary	French Society of Pharmacology and Therapeutic Association of Teachers of Pharmacology
	Pubmed
Classifications and terminology	Anatomical Therapeutic Chemical Classification System
	CISMEF
Other rules repositories	Vidal Expert Vigilanz

In scientific references

*Strong fixation of VKA (90 to 99%) in **plasma albumin**, only the free form is active.*

***Many Drug interactions are observed with VKA**.*

1.Drugs that can potentiate anticoagulants

- Reducing the synthesis of vitamin K by the intestinal flora (antibiotic) or decreasing its intestinal absorption (paraffin oil);

*- By moving the K antivitamin related to its vector protein (**albumin**), thus increasing free active fraction (clofibrate-sulfonamide-NSAIDs);*

-

2. Drugs that can inhibit the effect of anticoagulants

*- Reducing their **intestinal absorption** (antacids, laxatives, Questran);*

- Increasing their metabolism liver enzyme induction (barbiturates, Tegretol, carbamates, griseofulvin, rifampicin);

- A diet rich in vitamin K (liver, cabbage, spinach ...) reduces the effectiveness of AVK.

Validation of the association rules

- Test of the validity of the rules in other environments (hospital / department)
  - Confidence Coefficient in all environments

Effect	Condition(s)	REGIONH	DENAIN MED A	DENAIN MED B	DENAIN CHIR	DENAIN GYN	ROUEN
appearance of low inr[Lab]	Lab(high inr)=1 MedInfo(age)>75 Lab(hypoalbuminemia)=1	7/12=58%	2/2=100%	2/3=66%	2/7=28%	no stay matches the causes	6/8=75%

- To date: over 50 rules validated

Methods

- Selection of a sample of 40 normal 40 abnormal stays
- 2 hospitals (region H DK, and Denain, Fr)
- Data available:
  - All the data incorporated in the data model and used for the data mining process
  - Plus the discharge letter
  - Available through the IDEEA viewer system

Ideal results would be:

Data Mining "normal" stays			
	Stay ID	Expert A	Expert B
DM "normal" stays	713	No AE	No AE
	47	No AE	No AE
	2458	No AE	No AE
	320	No AE	No AE
	1976	No AE	No AE
	25	No AE	No AE
	1400	No AE	No AE
	1850	No AE	No AE
	524	No AE	No AE
	823	No AE	No AE

Data Mining "Abnormal" stays			
	Stay ID	Expert A	Expert B
R+ E+ A-	5	pADE	pADE
	414	pADE	pADE
	1854	pADE	pADE
	913	pADE	pADE
	1031	pADE	pADE
	1724	pADE	pADE
R+ E+ A+	520	pADE	pADE
	1268	pADE	pADE
	297	AE	pADE
	1339	pADE	pADE

Actual results:
DM « normal » stays vs. experts' judgment

DM "normal" stays	Stay ID	Expert A	Expert B
	713	No AE	No AE
	47	No AE	No AE
	2458	No AE	No AE
	320	No AE	No AE
	1976	No AE	No AE
	25	No AE	No AE
	823	pADE	pADE
	1850	pADE	pADE
	524	pADE	pADE
	1400	ADE	No AE

} ADE BEFORE hospitalization

Region H stays
1 / 6 / 13

Data Mining "Normal" stays	Stay ID	Expert A	Expert B
	475947	No AE	No AE
	481688	No AE	No AE
	484325	No AE	No AE
	496390	No AE	No AE
	531491	No AE	No AE
	533792	No AE	No AE
	556550	No AE	No AE
	576219	No AE	No AE
	612356	No AE	No AE
	627513	No AE	No AE
	634858	No AE	No AE
	454299	No AE	Answ. Imp
	437529	No AE	AE
	509110	ADE	No AE
	439932	ADE	ADE

Denain stays
3 / 30

- Good inter-experts agreement
- Good DM-Experts agreement

DM « abnormal » stays vs. experts' judgment

DM "Abnormal" stays	Stay ID	Expert A	Expert B
	1031	ADE	ADE
	1339	ADE	ADE
	1724	ADE	ADE
	297	AE	ADE
	414	ADE	No AE
	913	ADE	No AE
	1854	ADE	No AE
	1268	No AE	ADE
	5	No AE	No AE
	520	No AE	No AE

Region H stays

8 / 1 / 11

Data Mining "Abnormal stays	Stay ID	Expert A	Expert B
	445174	ADE	ADE
	460688	ADE	ADE
	486149	ADE	ADE
	512205	ADE	ADE
	540415	ADE	ADE
	573050	ADE	ADE
	595790	ADE	ADE
	636842	ADE	ADE
	477670	Answ. Imp	ADE
	536349	ADE	Answ. Imp
	538661	ADE	Answ. Imp
	637540	Answ. Imp	ADE
	451530	No AE	ADE
	472778	No AE	ADE
	476906	No AE	ADE
	483446	No AE	ADE
	550554	No AE	ADE
	637073	No AE	ADE
	635522	ADE	No AE
	452373	No AE	AE
	629360	No AE	Answ. Imp
	446122	No AE	No AE

Denain stays

11 / 6 / 27

- (1) Moderate inter-experts agreement
- (2) Correct to moderate DM-experts agreement

Current status of the Validation process

- Currently: 600 Decision Trees
- Hundreds of rules
- Validation in progress: 250 rules are validated

Scientific goals

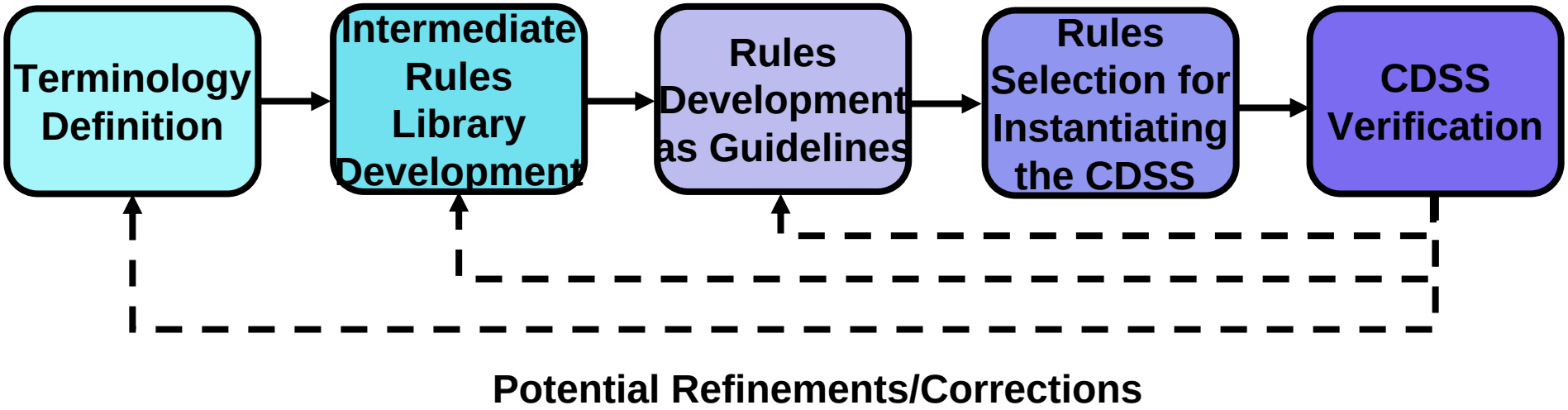
– **Identification** of ADEs

- « To get a better knowledge of the prevalence of Adverse Drug Events (ADEs) and of their characteristics per hospital, per Region, per Country »

– **Prevention** of ADEs

- « To develop concepts and methods to achieve the contextualization of CDSS (alerting) functions »

Implementation Procedure Followed



Current Results (R) and Expectations (E)

- R: A **first release of the PSIP terminology** has been defined

  E: Terminology evolution considering also ADE taxonomies

- R: A large **library of intermediate rules** has been developed as well as a **representative portion of rules** originated from data mining via **automated scripts** and **manually** respectively

  E: Support for **fully automated rule implementation**

- R: Semi-automated **rule verification mechanism** implemented

  E: Implement **additional knowledge management tools**

- R: 1st experiments on KB contextualization

  E: Development of advanced contextualized CDSS

☞ Final outcome: Interoperable, manageable and contextualised CDSS for ADE prevention

Research Challenges

- Approaches for **contextualizing** the KB, e.g. profiling, and consequently the decision support functionality
- **Knowledge maintenance**: policies and mechanisms for **updating** rules, **consistency checking**, **conflict resolution**, etc
- **Prioritization** of rules to avoid **over-alerting** and increase effectiveness
- **CDSS validation** issues
- Encoding **human factors** originated **knowledge**
- **Knowledge interoperability**: KB encoding and accessibility issues
- **Reusability**: Encoding of rules in RuleML, R2ML, etc
- **Interfacing** the healthcare IT infrastructure with the CDSS

Conclusion

- Promising results
- From data mining to CDSS
- Importance of the contextualization
- Importance of Human and organisational factors (avoid over-alerting)

- Time is short
- Legal constraints
- Integration in a more global quality inssurance process