Supporting Guideline-Based Treatments for Polypathological Patients

Gersende Georg [1], Brigitte Séroussi[1,2], and Jacques Bouaud[1,2]

[1]Inserm ERM 202, Paris, France
&
[2]STIM, DPA / DSI / AP – HP, Paris, France

Medinfo 2004, San Francisco, USA, 10 September 2004.

Outline

- Context of the work
  - Single-disease guideline recommendations
  - Problems encountered for polypathological patient
- Technical approach
  - Rule base derivation
  - Inference engine
    - Pattern matching
    - Synthesis of recommendations
- Conclusion

Medical context

- Clinical Practice Guidelines (CPGs)
  - General descriptions of “ideal” patients
  - Focusing on one disease only

- Problem:

  How do we choose the most appropriate therapeutics for polypathological patients using CPGs?

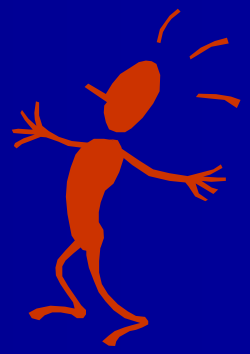
Single-disease guidelines recommendations

Ischemic heart disease

Recommendations

1. For patients with stable angina and hypertension, β-adrenergic antagonists are preferred as initial therapy (grade D).
2. Alternative therapies would include long-acting calcium-channel blockers (grade B). Short-acting calcium-channel blockers should not be used (grade C).
3. Patients with hypertension and a recent myocardial infarction should be treated with either β-adrenergic antagonists, ACE inhibitors or both. Both classes of drug protect against reinfarction and death (grade A).
4. Alternative therapies would include verapamil (grade A) and diltiazem (grade C), but only in the setting of normal left ventricular function.

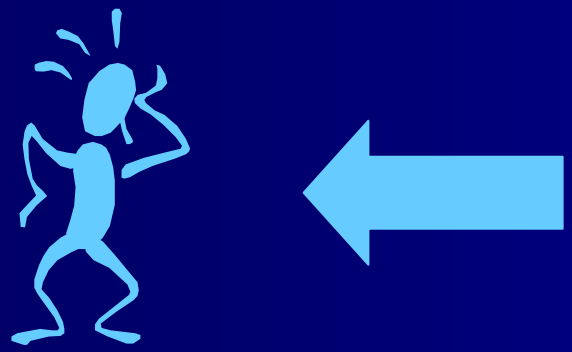
HT and stable angina



R_{T1} = BB

Single-disease guidelines recommendations

HT and renal disease



R_{T2} = ACE inhibitor

Renal disease

Recommendations

...

3. For patients with hypertension and renal disease, preferred initial therapy is with an ACE inhibitor (grade A).
4. Diuretics are recommended as additional antihypertensive therapy, since patients with renal insufficiency usually have difficulty with sodium balance (grade D).
5. Dihydropyridine calcium-channel blockers are recommended as alternative therapy for renoprotection in patients with nondiabetic renal disease (grade B).

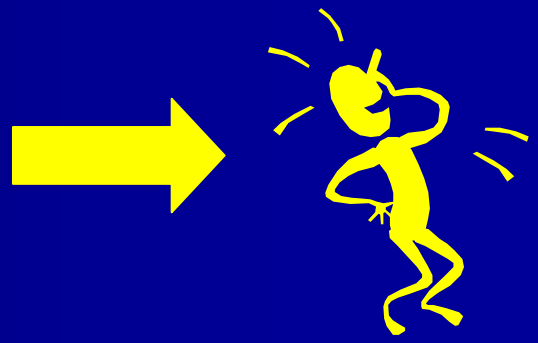
Single-disease guidelines recommendations

Systolic dysfunction

Recommendations

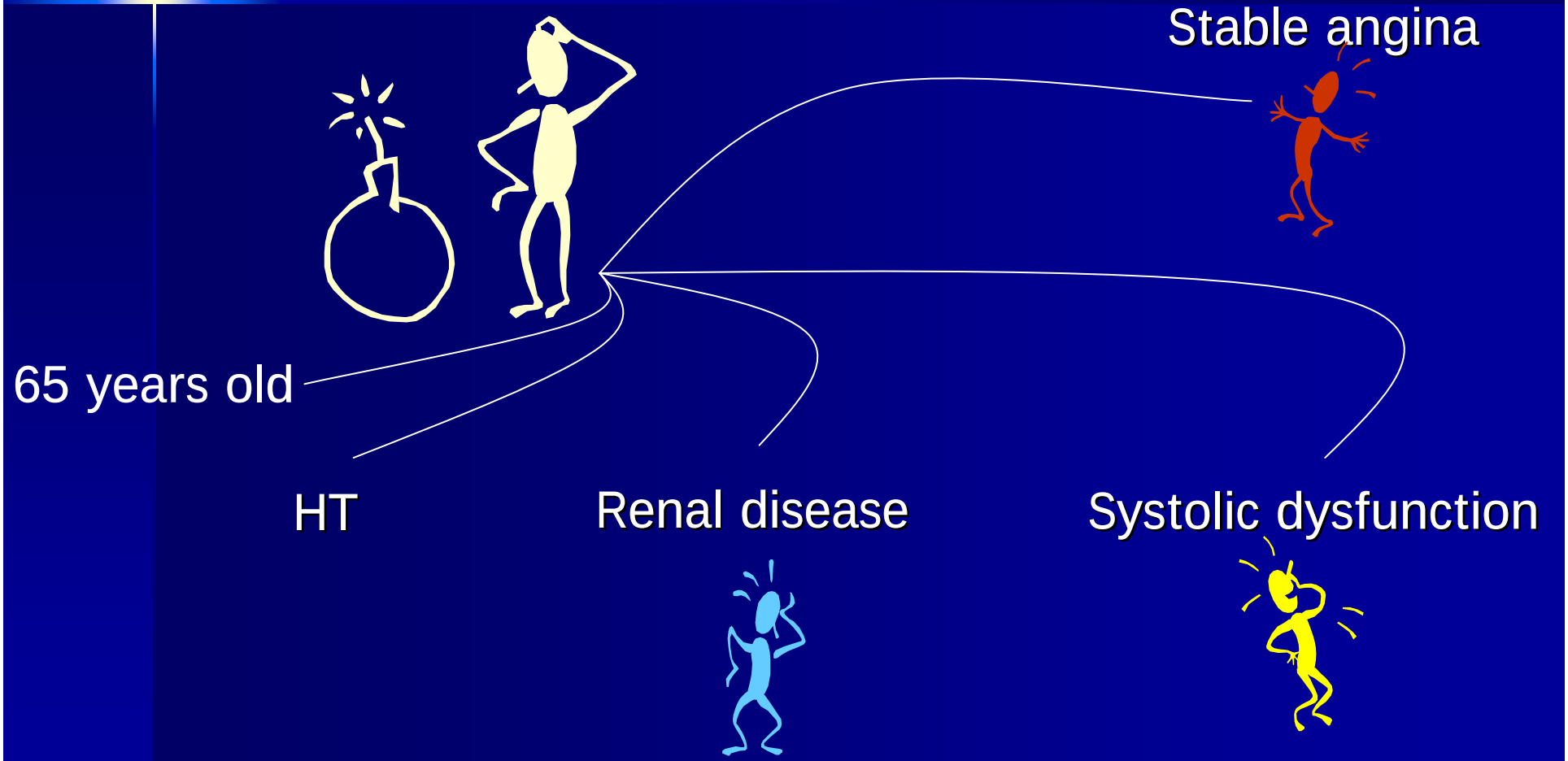
1. In patients with hypertension and systolic dysfunction, ACE inhibitors are recommended for initial therapy (grade A). Diuretics are recommended as additional therapy (grade A for thiazide diuretcis, grade D for loop diuretics).
2. A combination of hydralazine and isosorbide dinitrate (grade A) or an angiotensin II receptor antagonist (grade A in patients older than 65 years of age) is recommended as an alternative therapy.
3. For patients with left ventricular systolic dysfunction who remain hypertensive despite optimal doses of ACE inhibitors or alternative first-line therapies, additional therapies would include β-adrenergic blockade with either carvedilol (grade A), or metoprolol (grade A) or the long-acting dihydropyridine calciumchannel blockers amlodipine (grade A) or felodipine (grade B).

HT and systolic dysfunction

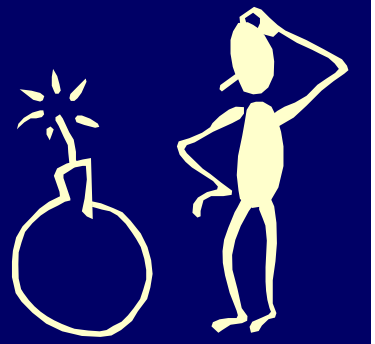


R_{T3} = ACE inhibitors

A polypathological patient



What's the best treatment???



HT with stable angina

R_{T1} = BB

HT with renal disease

R_{T2} = ACE inhibitors

HT with systolic dysfunction

R_{T3} = ACE inhibitors

R_{T1}? R_{T2}? R_{T3}?

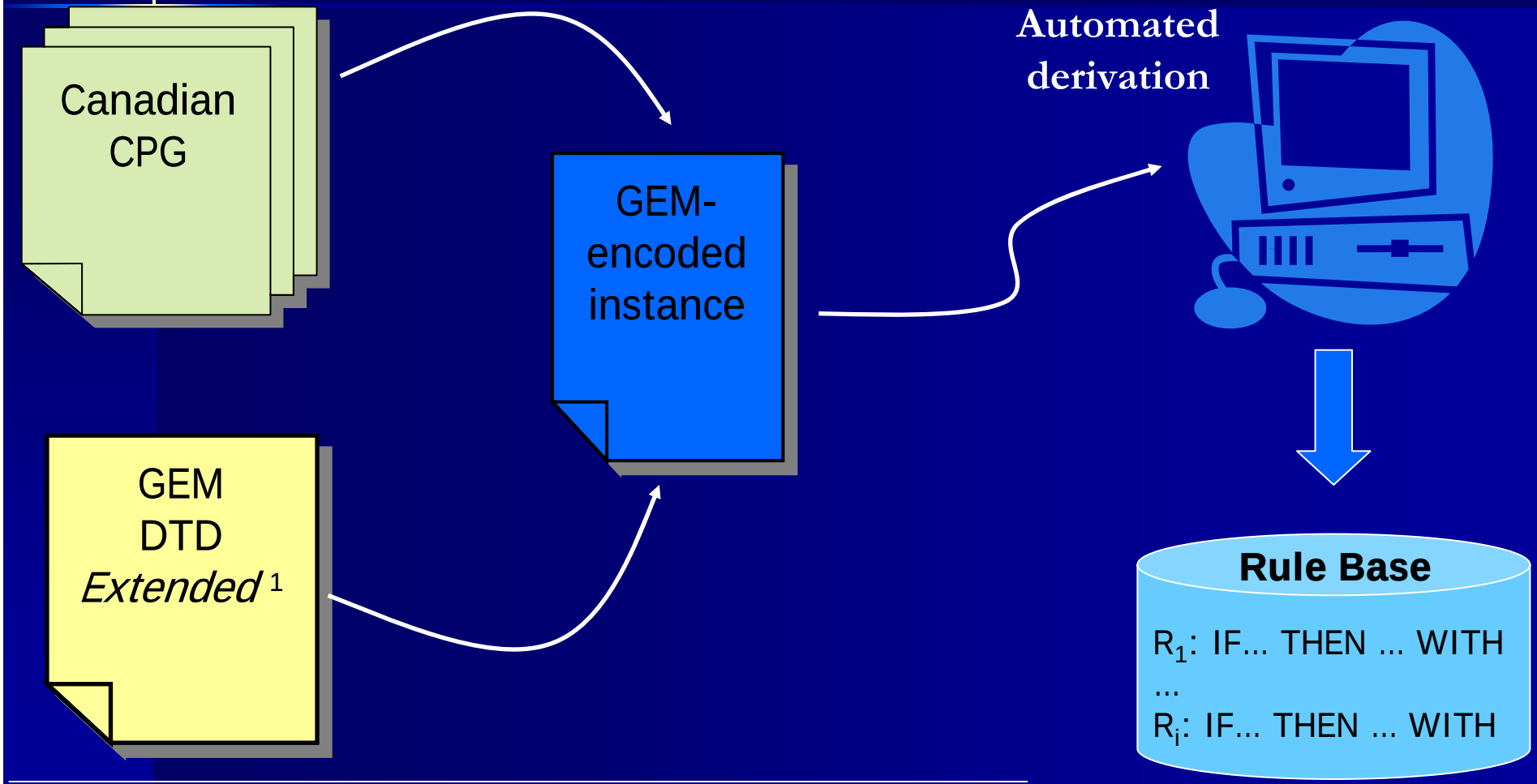
$R_{T1} \wedge R_{T2}$? $R_{T1} \wedge R_{T3}$?

$R_{T1} \wedge R_{T2} \wedge R_{T3}$?

Key ideas

- Automatic extraction (from textual CPG) of therapeutic rules addressing clinical situations (one disease, two associated diseases)
- Using the rule formalism to synthesize the contents of several sections and aggregate recommendations for multiple diseases (>2)

Deriving a rule base from textual guidelines



[1] Georg G, et al. Extending the GEM model to support knowledge extraction from textual guidelines. International Journal of Medical Informatics, In Press.

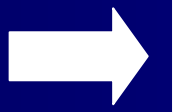
Creation of a GEM-encoded instance

- XML marking-up of CPG documents
- GEM[1]
  - Guideline document model of CPGs
  - Defines a structure for basic units of information
  - Multi-level hierarchy of more than 100 elements
- Extension of GEM
  - Add additional level of structuring supporting rule generation

[1]Shiffman RN, et al. GEM: a proposal for a more comprehensive guideline document model using XML. *J Am Med Inform Assoc* 2000;7(5):488-498.

The GEM-encoded instance

For patients with hypertension and renal disease, preferred initial therapy is with an ACE inhibitor (grade A).



<decision.variable source="explicit"
decision.variable.id="state_patient.pathology">HT
<value source="implicit" id="HT"/> </decision.variable>

<decision.variable source="explicit"
decision.variable.id="state_patient.pathology">renal disease
<value source="implicit"
id="REN_DIS"/></decision.variable>

<action source="explicit" id="treatment.line">first line treatment
<value source="implicit" id="L1"/> </action>

<action source="explicit" id="treatment.intention">first intention
<value source="implicit" id="INT1"/> </action>

<action source="explicit" id="treatment.type">monotherapy
<value source="implicit" id="MONO"/> </action>

<action source="explicit" id="treatment.nature">ACE inhibitor
<value source="implicit" id="ACE_in"/> </action>

<recommendation.strength source="explicit" id="A">grade A
< recommendation.strength>

The Rule formalism

IF $[C \wedge T]$ **THEN** R_T **WITH** Context

$[C \wedge T]$:

- Set of clinical criteria $C=\{C_i\}$
- Set of therapeutic criteria $T=\{T_j\}$

→ Value of *decision.variable* elements

R_T

- Therapeutic recommendation

→ Value of *action* elements

Context:

strength $\wedge$ *character* $\wedge$ *sign*

Strength: A, B, C, D
Character: D_Reco (grade=A);(Dominant=true), N_Reco, R_Reco
Sign: +/-

Automatic derivation of rules

<decision.variable source="explicit" decision.variable.id="state_patient.pathology"> HT
<value source="implicit" id="HT"/>
</decision.variable>

<decision.variable source="explicit" decision.variable.id="state_patient.pathology"> renal disease
<value source="implicit" id="REN_DIS"/>
</decision.variable>

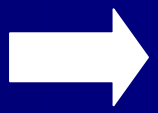
<action source="explicit" id="treatment.line">first line treatment
<value source="implicit" id="L1"/> </action>

<action source="explicit" id="treatment.intention">first intention
<value source="implicit" id="INT1"/> </action>

<action source="explicit" id="treatment.type">monotherapy
<value source="implicit" id="MONO"/> </action>

<action source="explicit" id="treatment.nature"> ACE inhibitor
<value source="implicit" id="ACE_in"/> </action>

<recommendation.strength source="explicit" id="A">grade A <recommendation.strength>

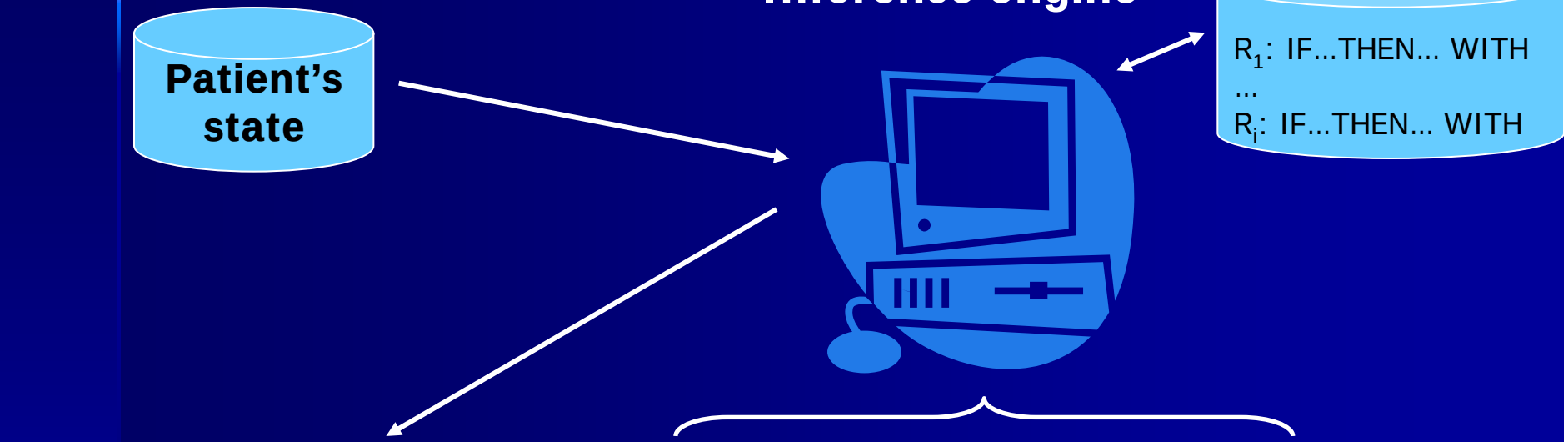


IF
patient_state.pathology = HT
and patient_state.pathology = REN_DIS

THEN
treatment.line = L1
and treatment.intention = INT1
and treatment.type = MONO
and treatment.nature = ACE_in

WITH
recommendation.strength = A
and character = D_Reco
and sign = +

Extraction of applicable relevant rules



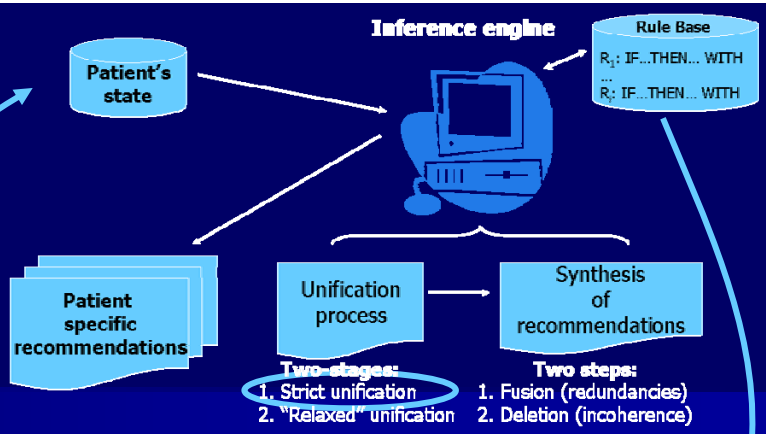
Two-stages:

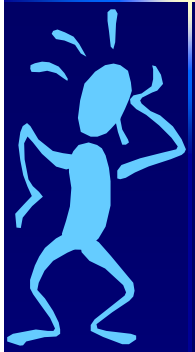
1. Strict unification
2. "Relaxed" unification

Two steps:

1. Fusion (redundancies)
2. Deletion (incoherence)

Strict unification





state_patient.pathology = HT

$\wedge$ state_patient.pathology = REN_DIS

R_{145}: ...

THEN treatment.line=L1

$\wedge$ treatment.intention=INT1

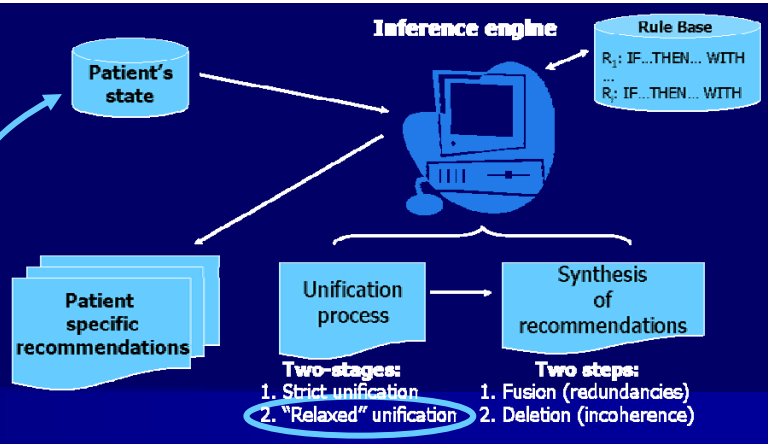
$\wedge$ treatment.type=MONO

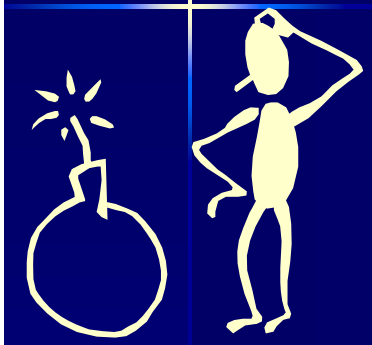
$\wedge$ treatment.nature=ACE_in

WITH A $\wedge$ D_Reco $\wedge$ +

ACE inhibitor with grade A

“Relaxed” unification

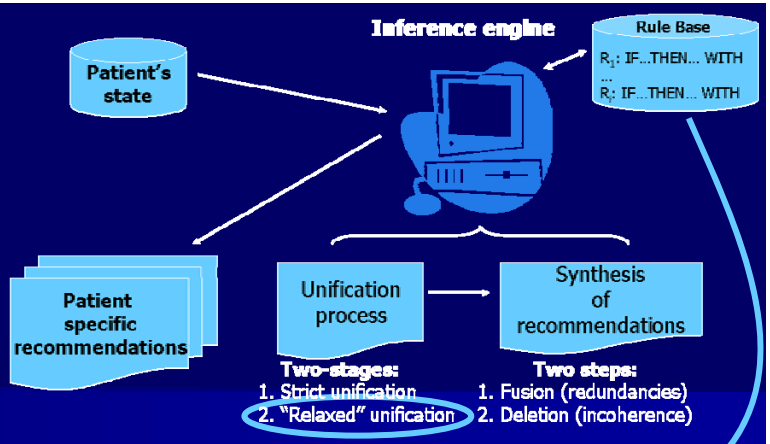




state_patient.age = 65

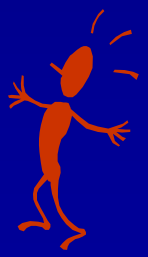
- ∧ state_patient.pathology = HT
- ∧ state_patient.pathology = REN_DIS
- ∧ state_patient.pathology = ISC_HEA_DIS
- ∧ state_patient.pathology = STA_ANG
- ∧ state_patient_pathology = SYS_DYS

Which are applicable recommendations?



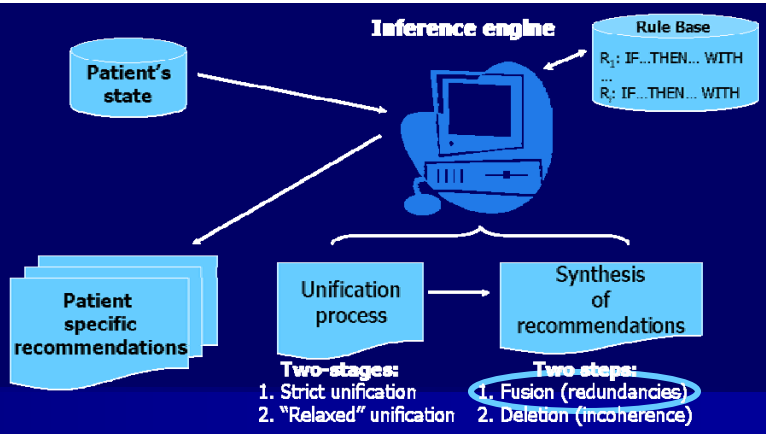
R_{145}: ...
THEN treatment.line=L1
∧ treatment.intention=INT1
∧ treatment.type=MONO
∧ treatment.nature=ACE_in
WITH A ∧ D_Reco ∧ +

R_{47}: ...
THEN treatment.line=L1
∧ treatment.intention=INT1
∧ treatment.type=MONO
∧ treatment.nature=ACE_in
WITH A ∧ D_Reco ∧ +



R_{70}: ...
THEN treatment.line=L1
∧ treatment.intention=INT1
∧ treatment.type=MONO
∧ treatment.nature=BB
WITH D ∧ D_Reco ∧ +

Elimination of redundancies (Fusion)

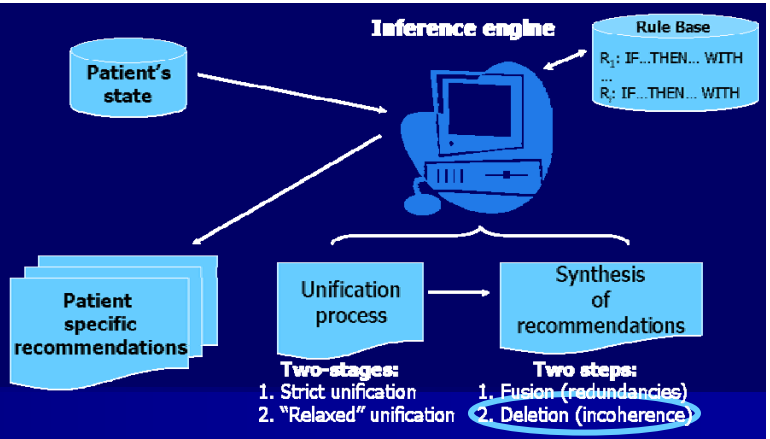


R_{145}: ...
THEN treatment.line = L1
∧ treatment.intention = INT1
∧ treatment.type = MONO
∧ treatment.nature = ACE_in
WITH A ∧ D_Reco ∧ +

R_{47}: ...
THEN treatment.line = L1
∧ treatment.intention = INT1
∧ treatment.type = MONO
∧ treatment.nature = ACE_in
WITH A ∧ D_Reco ∧ +

Recommendations are merged into a unique recommendation of ACE inhibitors, with grade = A *and* character = D_Reco *and* sign = +

Elimination of inconsistencies (Deletion)

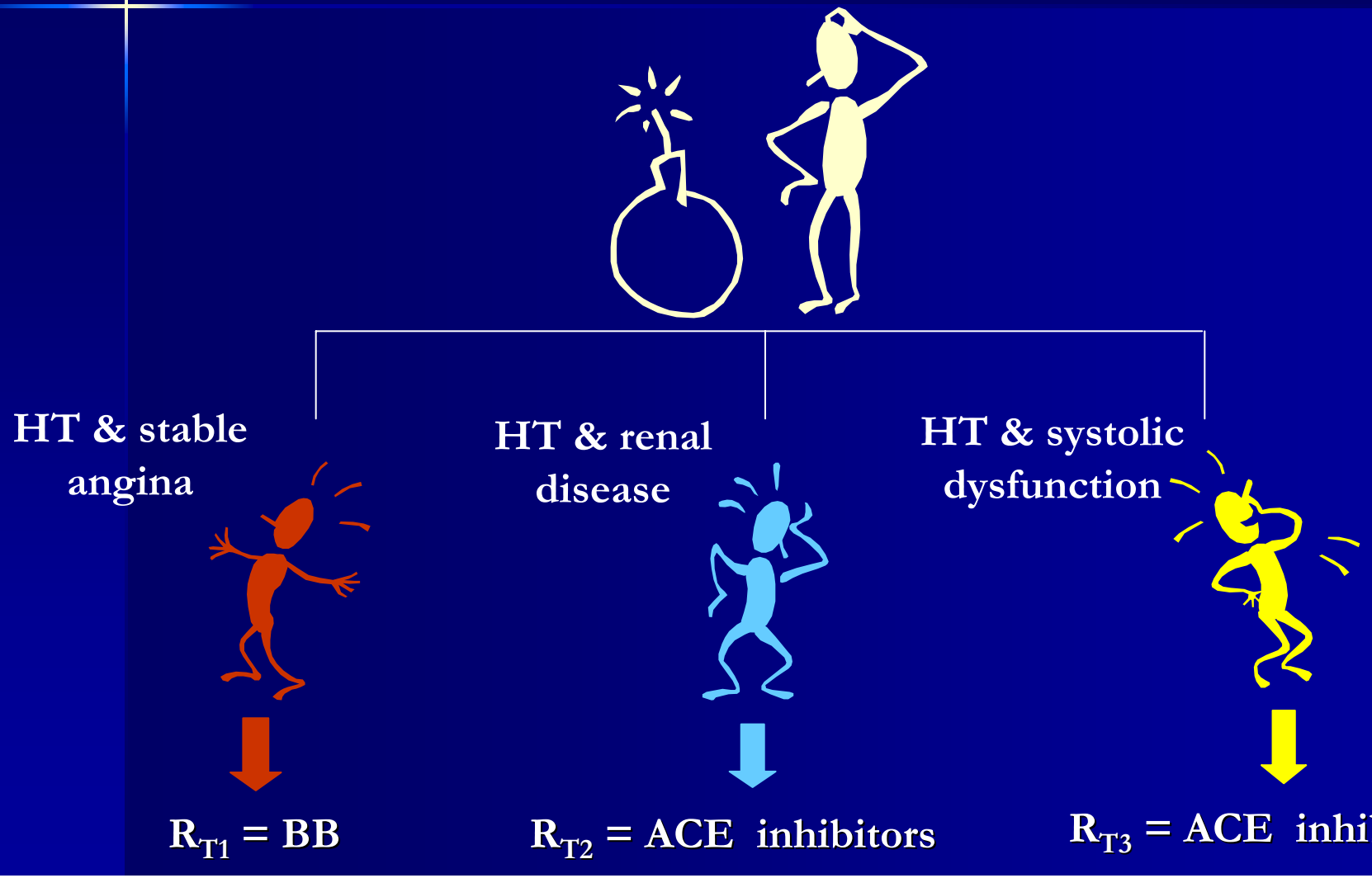


IF
patient_state.pathology = HT
∧ patient_state.pathology = ISC_HEA_DIS
∧ patient_state.pathology = STA_ANG
THEN
treatment.line = L1
∧ treatment.intention = INT1
∧ treatment.type = MONO
∧ treatment.nature = BB
WITH
D ∧ D_Reco ∧ **+**

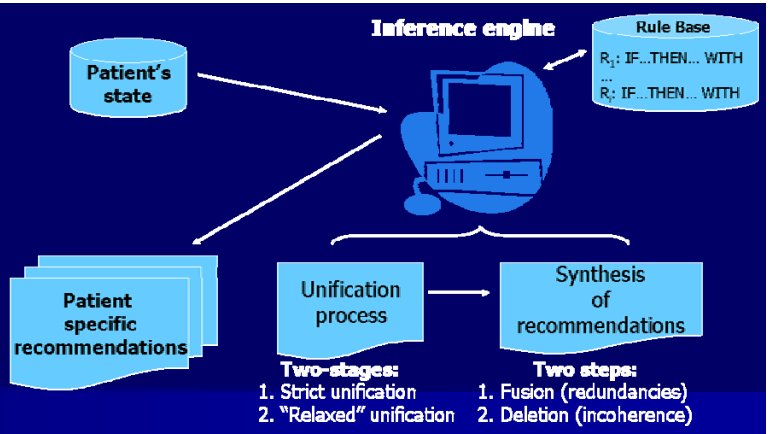
IF
patient_state.pathology = HT
∧ patient_state.pathology = REV_AIRWAY_DIS
THEN
treatment.line = L1
∧ treatment.intention = INT1
∧ treatment.type = MONO
∧ treatment.nature = BB
WITH
D ∧ D_Reco ∧ **-**

Recommendations are cancelled and BB are eliminated for final recommendations

Decomposing the patient into "virtual" individual patients

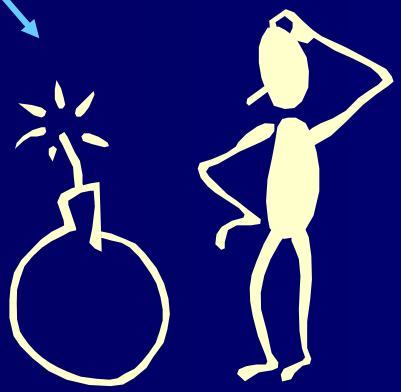


Patient specific recommendations



ACE inhibitors (grade A) ---- source ----> HT & renal disease & systolic dysfunction

BB (grade D) ---- source ----> HT & ischemic heart disease & stable angina



Physician's choice ⟹ ACE inhibitors (grade A)

Conclusions

- From guidelines: “Ideal case” or “textbook patient”
  - Guidelines describe an “ideal” patient suffering from only one associated disease in addition to the guideline’s main disease (here hypertension)
- How do we manage “real”-world patients?
  - Decompose patient description into “virtual” individual patients affected by a single disease
  - Trigger rules containing at least one disease
  - Synthesize rules
- Proposing of a set of applicable recommendations in context enables to physician the select of the best one