Quality Checking Medical Guidelines

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Health Care Computing

- NWO hefboom
- Part of LaQuSo
- Projects:
  - Breast cancer classification/detection
  - Finding pathways in gene expression data
  - Nuadu (tele-medicine)
  - Protocure (verification medical guidelines)

Protocure (www.protocure.com)

- Universitat Jaume I, Castellón, Spain
- Fundació Biblioteca Josep Laporte, Barcelona, Spain
- Vienna University of Technology, Vienna, Austria
- University of Augsburg, Augsburg, Germany
- Radboud Universiteit, Nijmegen, NL
- Vrije Universiteit, Amsterdam, NL
- Dutch Institute for Healthcare Improvement (CBO), Utrecht, NL

Medical Guidelines

- Evidence-based medicine
- Promoting standards of medical care

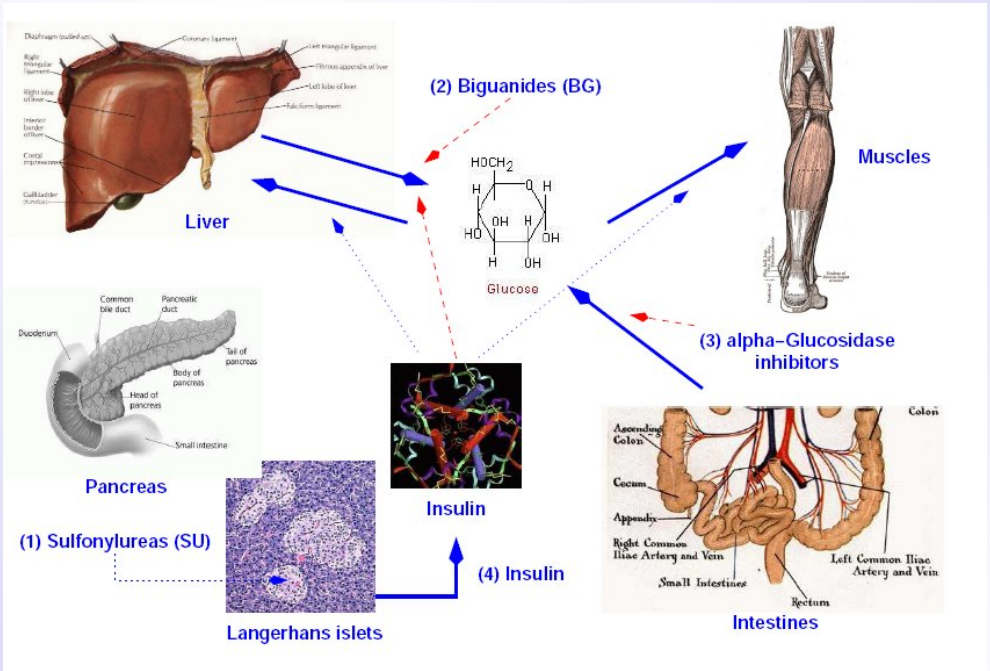
"Clinical practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific circumstances" [Field & Lohr, 1990].

Objective / Approach

Objective: Support guideline developers in the health-care profession in the construction and maintenance of high-quality and up-to-date living guidelines and protocols

Approach: Applying formal methods for quality checking medical guidelines

Diabetes Mellitus Type 2



Management DM-2

- Step 1: diet
- Step 2: if quetelet index ≤ 27, prescribe a sulfonylurea drug, otherwise prescribe a biguanide drug
- Step 3: combine a sulfonylurea drug and biguanide drug.
- Step 4: one of the following:
  - oral antidiabetic and insulin
  - only insulin

Temporal Logic

Notation	Interpretation	Formal semantics
$\Box\ \varphi$	φ will always be true	$t \vDash \Box\ \varphi \Leftrightarrow \forall t' \geq t : t' \vDash \varphi$
$\Diamond\ \varphi$	φ will eventually be true	$t \vDash \Diamond\ \varphi \Leftrightarrow \exists t' \geq t : t' \vDash \varphi$
φ **until** ψ	φ holds until ψ eventually holds	$t \vDash \varphi$ **until** ψ $\Leftrightarrow \exists\ t' \geq t :\ t' \vDash \psi$ $\wedge \forall\ t \leq t'' < t' : t'' \vDash \varphi$
φ **unless** ψ	φ holds unless ψ holds	$t \vDash \varphi$ **unless** ψ $\Leftrightarrow \forall\ t' \geq t :\ t' \vDash \varphi$ $\vee \exists\ t \leq t'' \leq t' : t'' \vDash \psi$
$\circ\ \varphi$	execution does not terminate and the next state satisfies φ	$t \vDash \circ\ \varphi \Leftrightarrow \exists\ t' \in \text{succ}(t) : t' \vDash \varphi$
$\bullet\ \varphi$	either execution terminates or the next state satisfies φ	$t \vDash \bullet\ \varphi \Leftrightarrow \forall\ t' \in \text{succ}(t) : t' \vDash \varphi$
last	the current state is the last	$t \vDash$ **last** $\Leftrightarrow \text{succ}(t) = \varnothing$

Background Knowledge

$\Box$ Drug(insulin) $\rightarrow \Box$ (uptake(liver,glucose) = up $\wedge$
uptake(peripheral-tissues,glucose) = up

$\Box$ Drug(SU) $\wedge \neg$ capacity(B-cells,insulin) = exhausted $\rightarrow$
$\Box$ secretion(B-cells,insulin) = up

$\Box$ Drug(BG) $\rightarrow \Box$ release(liver,glucose) = down

Quality Requirements of Treatments (1 of 2)

Let $\mathcal{B}$ be background knowledge, T be a treatment, P be a patient group, N be intensions:

Consistency: $\mathcal{B} \cup \Box T \cup P \not\models \bot$

Coverage: $\mathcal{B} \cup \Box T \cup P \models N$

- $T = \{SU, BG\}$
- $P = \{capacity(B\text{-}cells, insulin) = nearly\text{-}exhausted, Condition(hyperglycaemia)\}$
- $N = \{Condition(normoglycaemia)\}$

Quality Requirements of Treatments (2 of 2)

Optimality: $O_\varphi(T)$ holds, where O_φ is a meta-predicate standing for an optimality criterion or combination of optimality criteria φ defined as: $O_\varphi(T) \equiv \forall T' \in \mathsf{Pr}_P : T' \preceq_\varphi T$,

minimal insulin injections + minimal drugs:

$$
\begin{aligned}
\text{insulin} &\preceq_\varphi \text{insulin and antidiabetic} \\
&\preceq_\varphi \text{sulfonylurea and biguanide drug} \\
&\preceq_\varphi \text{sulfonylurea or biguanide drug} \\
&\preceq_\varphi \text{diet}
\end{aligned}
$$

Quality Requirements of Guidelines

Let in addition A be a guideline, then:

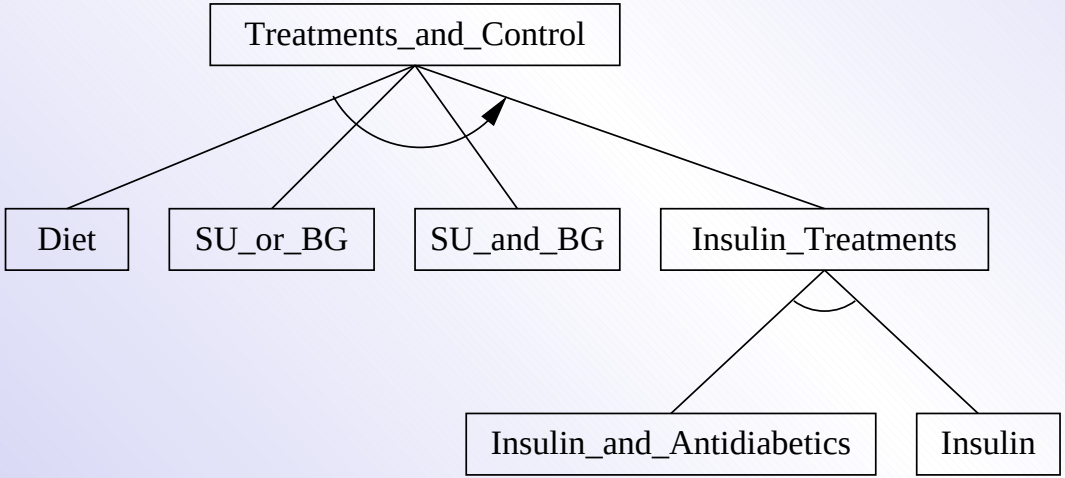
Consistency: $\mathcal{B} \cup A \cup P \not\models \bot$

Coverage: $\mathcal{B} \cup A \cup P \models \Diamond N$

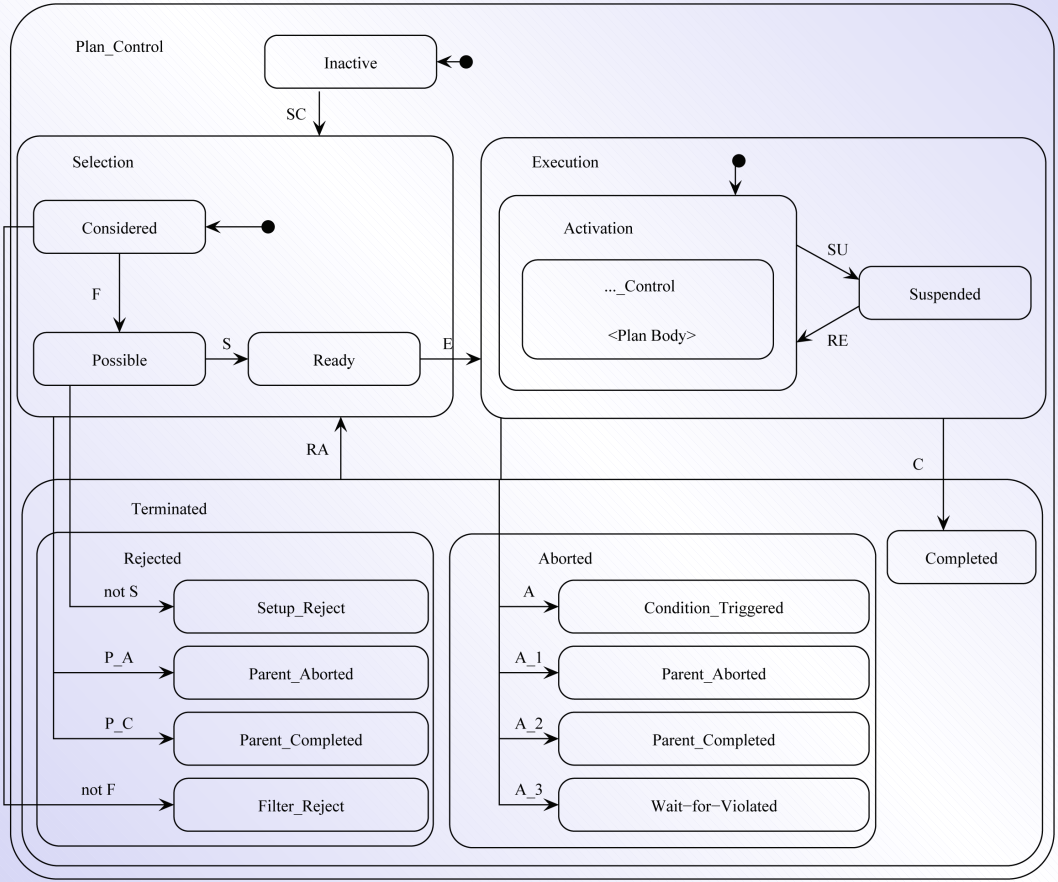
Optimality: $O_\varphi(A)$ holds, where O_φ is a meta-predicate standing for an optimality criterion or combination of optimality criteria φ defined as: $O_\varphi(A) \equiv \forall A' \in \mathsf{Pr}_P : A' \preceq_\varphi A$,

Asbru (1 of 2)

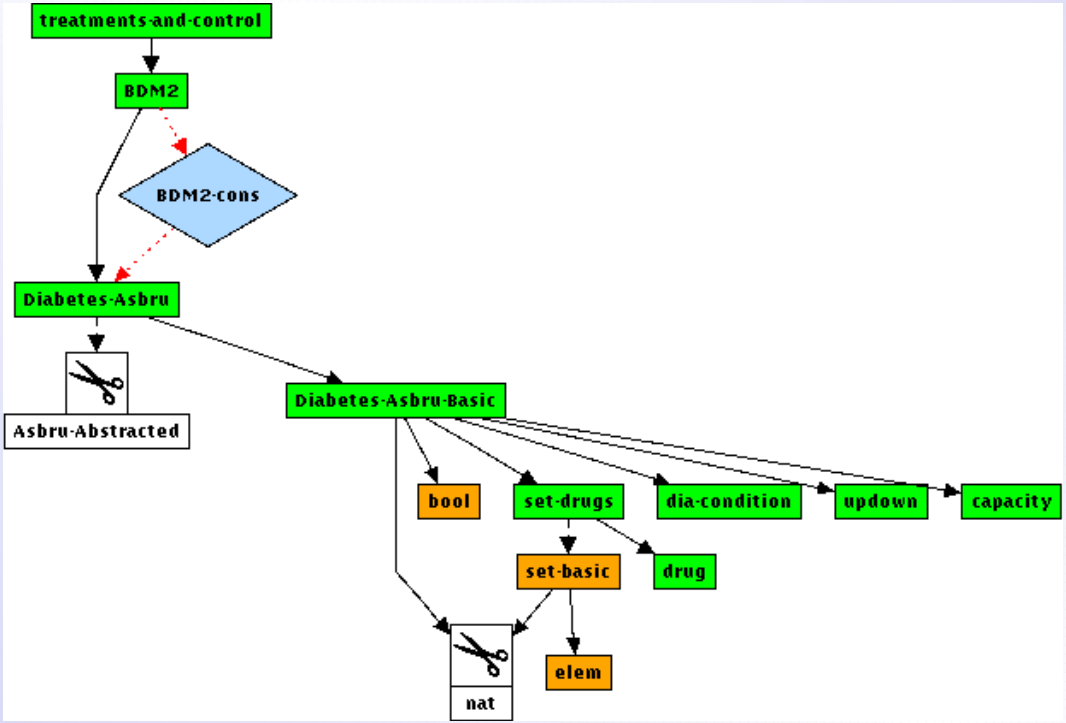
- Languages for a number of steps with a specific function or goal, e.g., PRO*forma*, Asbru, EON, GLIF, etc.



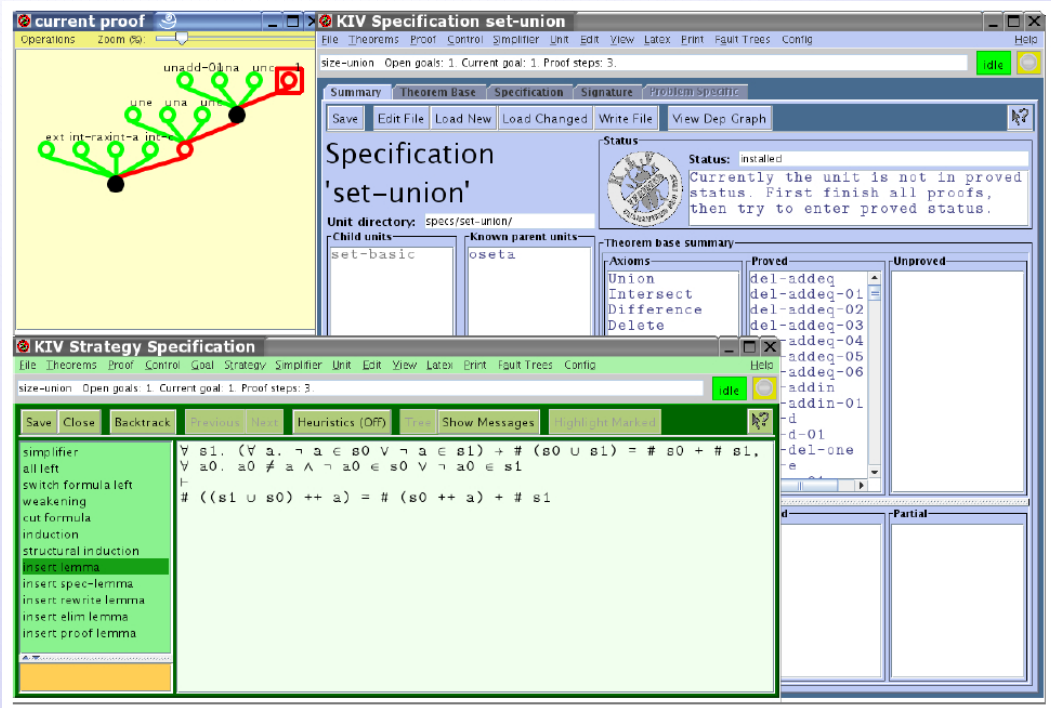
Asbru (2 of 2)


Plan_Control
Inactive
SC
Selection
Considered
F
Possible
S
Ready
E
Execution
Activation
..._Control
<Plan Body>
SU
Suspended
RE
RA
C
Terminated
Rejected
not S
Setup_Reject
P_A
Parent_Aborted
P_C
Parent_Completed
not F
Filter_Reject
Aborted
A
Condition_Triggered
A_1
Parent_Aborted
A_2
Parent_Completed
A_3
Wait−for−Violated
Completed

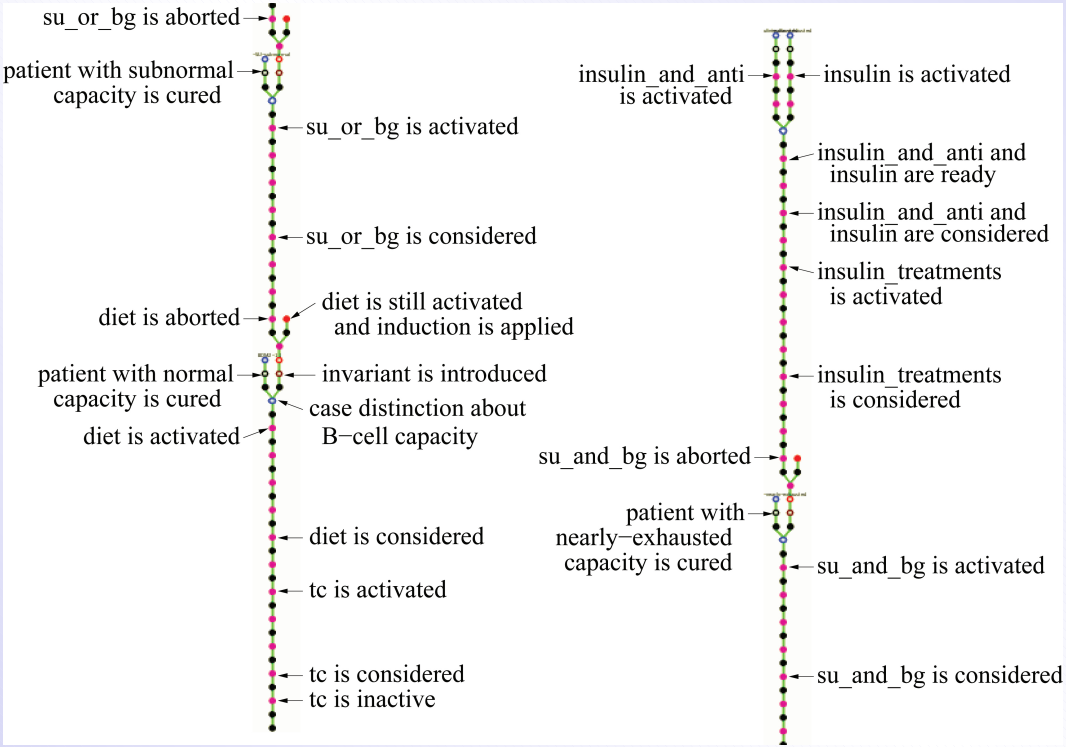
KIV (1 of 3)


treatments-and-control
BDM2
BDM2-cons
Diabetes-Asbru
Asbru-Abstracted
Diabetes-Asbru-Basic
bool
set-drugs
dia-condition
updown
capacity
set-basic
drug
elem
nat

KIV (2 of 3)


current proof
Operations
Zoom (%):
KIV Specification set-union
File Theorems Proof Control Simplifier Unit Edit View Latex Print Fault Trees Config
Help
size-union Open goals: 1. Current goal: 1. Proof steps: 3.
idle
Summary
Theorem Base
Specification
Signature
Problem Specific
Save
Edit File
Load New
Load Changed
Write File
View Dep Graph
Specification
'set-union'
Status
Status: installed
Currently the unit is not in proved status. First finish all proofs, then try to enter proved status.
Unit directory: specs/set-union/
Child units
set-basic
Known parent units
oseta
Theorem base summary
Axioms
Union
Intersect
Difference
Delete
Proved
del-addeq
del-addeq-01
del-addeq-02
del-addeq-03
del-addeq-04
del-addeq-05
del-addeq-06
addin
addin-01
d
d-01
del-one
e
Unproved
Partial
KIV Strategy Specification
File Theorems Proof Control Goal Strategy Simplifier Unit Edit View Latex Print Fault Trees Config
Help
size-union Open goals: 1. Current goal: 1. Proof steps: 3.
idle
Save
Close
Backtrack
Previous
Next
Heuristics (Off)
Tree
Show Messages
Highlight Marked
simplifier
all left
switch formula left
weakening
cut formula
induction
structural induction
insert lemma
insert spec-lemma
insert rewrite lemma
insert elim lemma
insert proof lemma
∀ s1. (∀ a. ¬ a ∈ s0 ∨ ¬ a ∈ s1) → # (s0 ∪ s1) = # s0 + # s1,
∀ a0. a0 ≠ a ∧ ¬ a0 ∈ s0 ∨ ¬ a0 ∈ s1
⊢
((s1 ∪ s0) ++ a) = # (s0 ++ a) + # s1

KIV (3 of 3)


su_or_bg is aborted
patient with subnormal capacity is cured
su_or_bg is activated
su_or_bg is considered
diet is aborted
diet is still activated and induction is applied
patient with normal capacity is cured
invariant is introduced
case distinction about B−cell capacity
diet is activated
diet is considered
tc is activated
tc is considered
tc is inactive
insulin_and_anti is activated
insulin is activated
insulin_and_anti and insulin are ready
insulin_and_anti and insulin are considered
insulin_treatments is activated
insulin_treatments is considered
su_and_bg is aborted
patient with nearly−exhausted capacity is cured
su_and_bg is activated
su_and_bg is considered