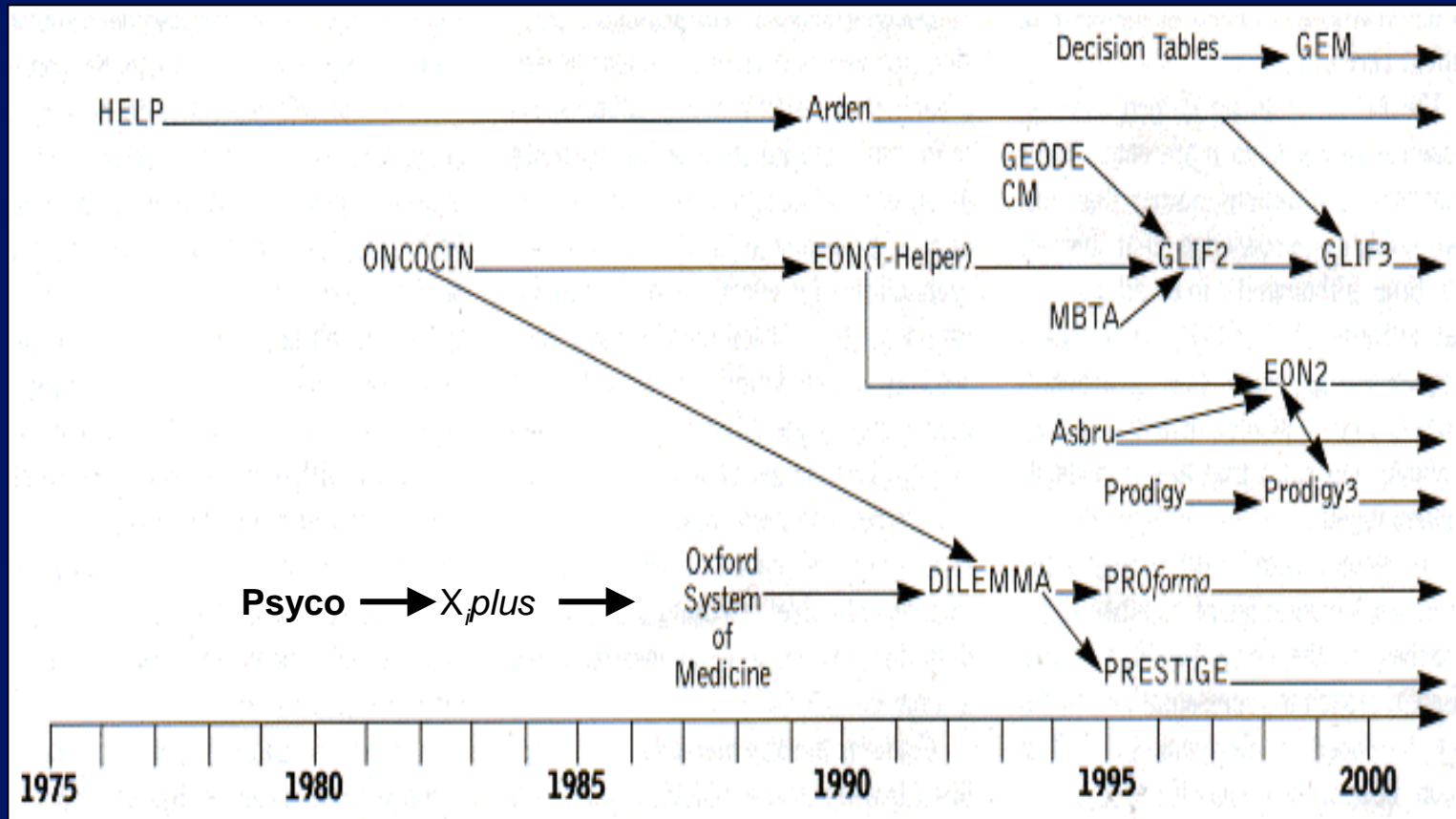


PRO*forma* progress

John Fox, Jon Bury, Michael Humber,
Ali Rahmanzadeh, Margarita Sordo

REACT group

David Glasspool, Tito Castillo, Vicky Monaghan



Elkin, Peleg, Lacson, Tu, Boxwala, Greenes, and Shortliffe. "Toward Standardization of Electronic Guidelines".

MD Computing, Vol. 17, No. 6, 2000, pp. 39-44.

PROforma technology (MIE 96)

- FO logic language for modelling decision-making and workflow in uncertain and time-evolving environments
- Integrating rule-based, object-oriented and task-network paradigms
- Formal notation for specifying tasks and processes
- Graphical and CASE tools for authoring task networks
- Language has procedural as well as declarative reading, permitting machine enactment of PROforma specifications

PROforma “tasks”

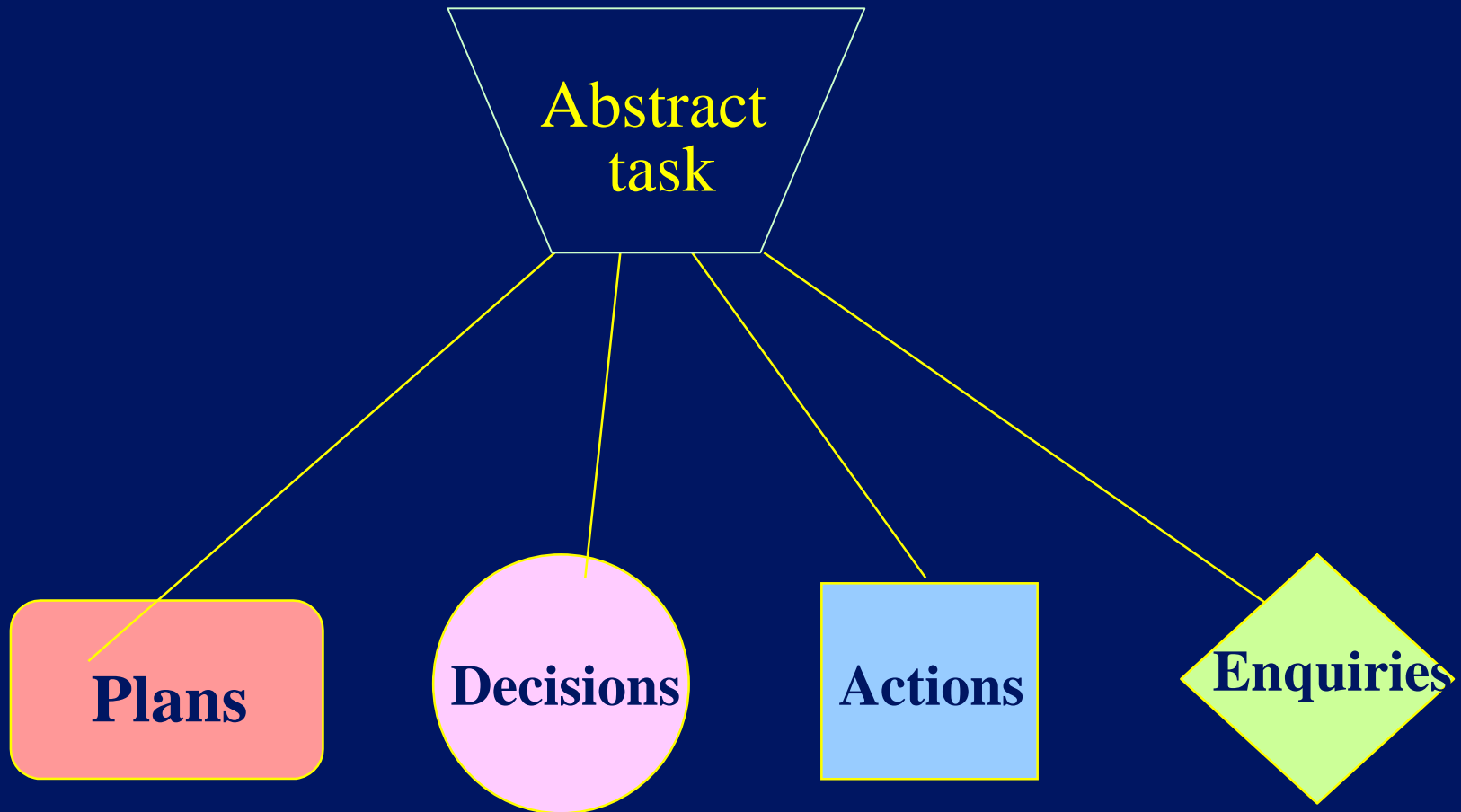
A task is an encapsulated body of knowledge designed to achieve a specific clinical objective, either in isolation or as a component of a more complex process. The knowledge encapsulated in a task typically includes both logical and control knowledge. A task can often be viewed as a module that may be reused across applications.

PROforma theory

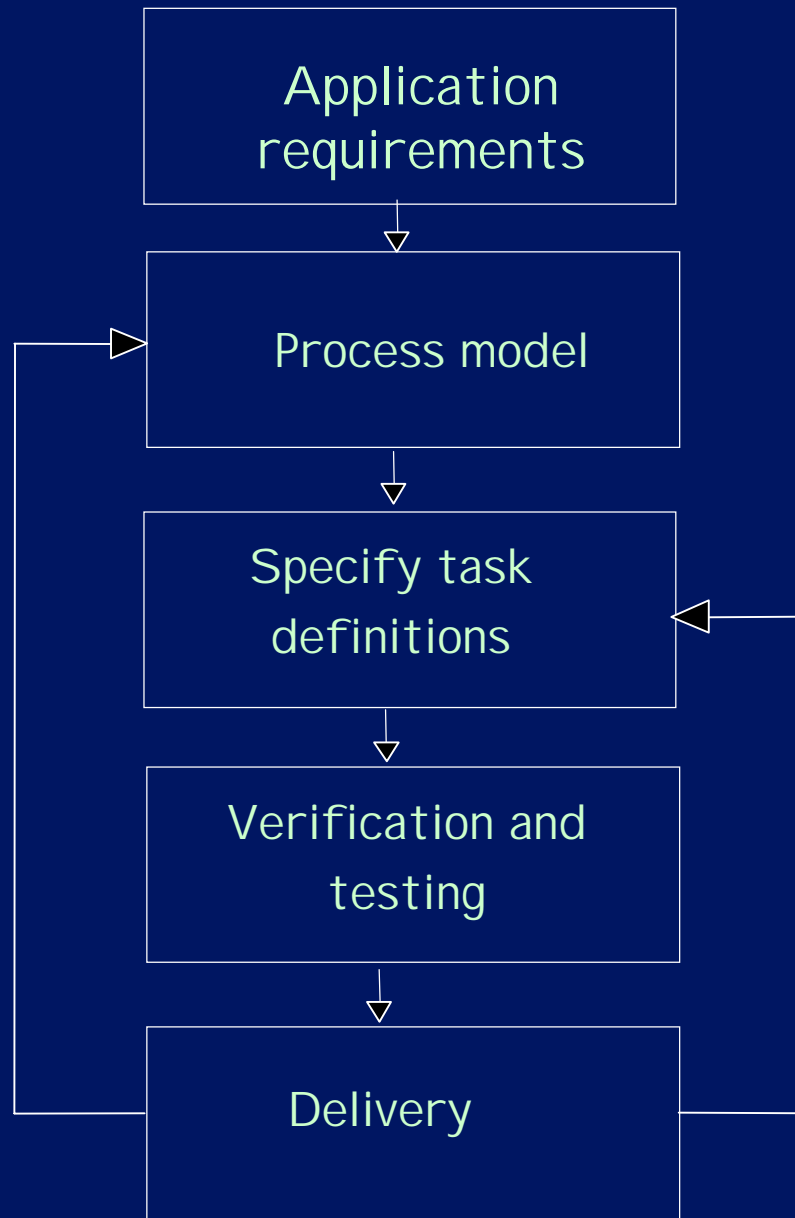
- Brings together ideas from mathematical logic, psychology of reasoning and judgement, and AI
- Clinical “agents” use an extended BDI model which supports task objects, decision making under uncertainty, plan enactment
- Formalised in terms of classical and non-classical logics

Fox and Das, *Safe and Sound*, MIT Press 2000

“Minimal” task ontology



PROforma development lifecycle



Arezzo® toolset

- Well engineered development environment
 - Graphical authoring tool
 - Ontology modeller
 - Enactment engine
 - Syntax-directed editor and model-checker
 - Integrated tester
- Arezzo 2i (2000) version supports web delivery and other refinements

AREZZO Composer

InferMed - Composer [Protocol1]
File Edit View Tools Help

- [-] Cancer risk assessment guideline
 - Personal history
 - Family history
 - enquiry3
 - Risk assessment
 - decision2
 - Exit guideline
- [-] Moderate risk pathway
 - Consent given
 - Do monitoring
 - Order screen
- [-] High risk pathway
 - Help
 - Quit

05/09/01 19:11

Hierarchical task view

```
/* Arezzo Guideline: Cancer_risk_assessment */  
/* 05/09/2001, 19:17:35 */  
  
plan :: Cancer_risk_assessment ;  
caption :: 'Cancer risk assessment guideline' ;  
component :: Personal_history ;  
component :: Family_history ;  
component :: enquiry3 ;  
component :: Risk_assessment ;  
  schedule_constraint :: completed(Personal_history) ;  
  schedule_constraint :: completed(Family_history) ;  
component :: decision2 ;  
  schedule_constraint :: completed(enquiry3) ;  
component :: action1 ;  
  schedule_constraint :: completed(Risk_assessment) ;  
  schedule_constraint :: completed(decision2) ;  
component :: Moderate_risk_pathway ;
```

Check Protocol

2 Errors
2 Warnings

ERROR 001 Enquiry: enquiry3
* Incomplete task definition - no sources defined

ERROR 002 Decision: decision2
* Incomplete task definition - no candidates defined

WARNING 001 Decision: decision2
- No recommendation rules defined

WARNING 002 Plan: High_risk_pathway
- No components in plan

Close

Arezzo decision editor

The image displays the 'Arezzo decision editor' interface, which is used for defining decision rules. The main window, titled 'Decision Editor on task: Risk_assessment', is divided into several sections:

- Sources:** A list of sources with 'Add' and 'Delete' buttons.
- Candidates:** A list of candidates with 'Add', 'Delete', and 'Edit' buttons. The 'elevated_risk' candidate is currently selected.
- Arguments for: elevated_risk:** A section for defining the argument condition, support level, and arguments list. The current condition is `for_count(first_degree_relatives_with_BrCa) >= 2`.
- Choice Mode:** Radio buttons for 'Mandatory' and 'Optional'.
- Support Mode:** Radio buttons for 'Symbolic Support' and 'Numeric Support'.

An overlay dialog titled 'Editing: A Decision's Argument Condition' is open, showing the current condition: `dateof(diagnosis) = _Date and date_diff(years, Date, datenow) |`. The dialog includes a rich text editor with a help text: 'The current date. datenow. Note that this value does not include time of day information.' Below the editor is a keyboard-style interface with buttons for mathematical operators, logical connectors, and functions. A numeric keypad is also present on the right side of the dialog.

Editing: A Decision's Argument Condition

dateof(diagnosis) = _Date and date_diff(years, Date, datenow) |

The current date.
datenow
Note that this value does not include time of day information.

+, -, *, /, ^, =, <>, >, >=, <, =<, [], ()

netsupport, result_of, and, or, not, case, else, like, between

count, average, sum, max, min, abs, if, isknown, status

now, datenow, timenow, dateof, datepart, date_diff, time_diff

any, oneof, start, date, first, isbefore, isafter, isduring

every, includes, end, time, last, before, after, during

&, ?, %, 7, 8, 9
:, ', ., 4, 5, 6
. 0, 1, 2, 3

OK Cancel

PROforma language syntax

- Formal specification language for modelling the process component of clinical expertise
- First-order language supporting
 - The concept of task (minimum ontology)
 - Data and concept definitions
 - Temporal expressions
 - Arithmetic and other common functions etc. etc.
- Syntax definitions available as
 - BNF
 - DTD

PROforma language semantics

- Support role or autonomous agents
 - BDI model augmented with temporal reasoning and uncertainty management
- Data and knowledge representation
 - Equiv to Horn clause logic (closed world negation)
 - Argumentation for decision making
 - Logic of obligation and time for scheduling
- Task enactment
 - Sequential or parallel pathways
 - Synchronous (scheduled) or asynchronous execution

Shared features with other reps

- Rules and functions encapsulated in tasks
- Tasks composed into time-oriented networks
- Nesting of processes (through plans)
- Support for seriality, concurrency, iteration
- Explicit support for decision making
- Interface primitives (actions, enquiries) through API

Distinctive features

- “Minimal” task ontology
- Focus on process, not patient data, ontological tools etc. (we aim to provide APIs for these)
- Concern with formal issues:
 - Clear semantics
 - Verification and validation
 - Explicit safety management
- Autonomous operation as well as support modes
- Generic agent model (not necessarily clinical)

Current ICRF research: Clinical applications

RAGs: Risk Assessment in Genetics

Andrew Coulson, David Glasspool

Jon Emery (CRC Fellow) and GPRG, Oxford



Patient Assessment Report

REFERRAL ADVICE

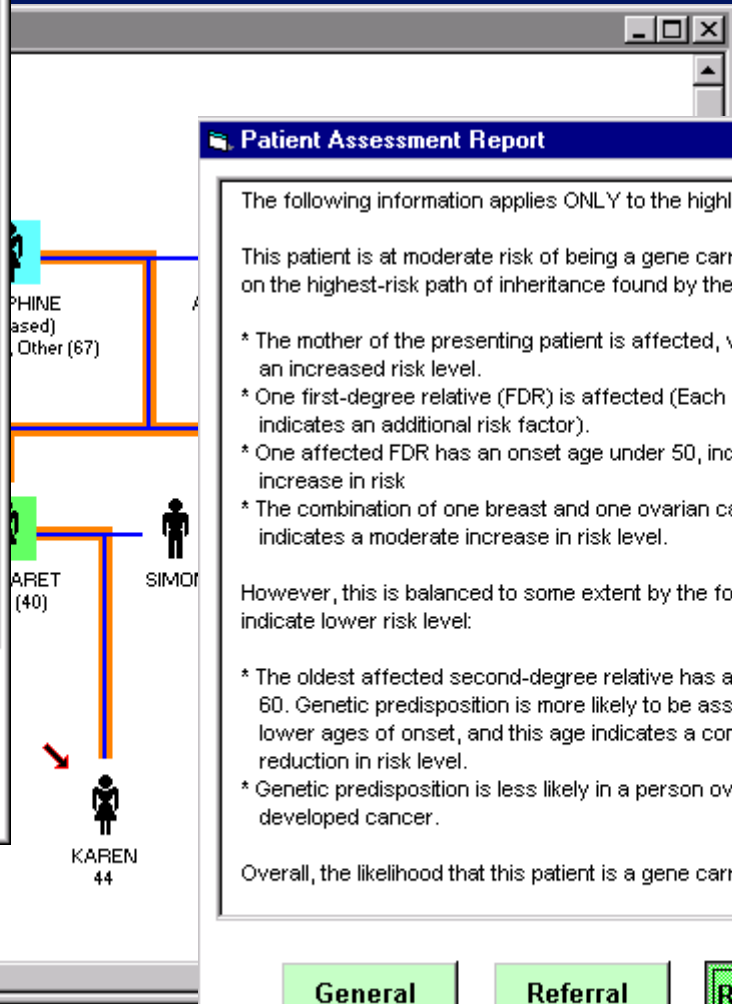
It would be appropriate to refer this patient to the breast clinic.

Currently it is unlikely that she will be a candidate for gene testing but additional screening for breast and/or ovarian cancer will be discussed.

**General
Explanation**

**Referral
Advice**

**Reasons for
Advice**



Patient Assessment Report

The following information applies ONLY to the highlighted path.

This patient is at moderate risk of being a gene carrier because, on the highest-risk path of inheritance found by the program:

- * The mother of the presenting patient is affected, which indicates an increased risk level.
- * One first-degree relative (FDR) is affected (Each affected FDR indicates an additional risk factor).
- * One affected FDR has an onset age under 50, indicating a moderate increase in risk
- * The combination of one breast and one ovarian cancer indicates a moderate increase in risk level.

However, this is balanced to some extent by the following factors which indicate lower risk level:

- * The oldest affected second-degree relative has an age of onset over 60. Genetic predisposition is more likely to be associated with lower ages of onset, and this age indicates a considerable reduction in risk level.
- * Genetic predisposition is less likely in a person over 40 who has not developed cancer.

Overall, the likelihood that this patient is a gene carrier is moderate.

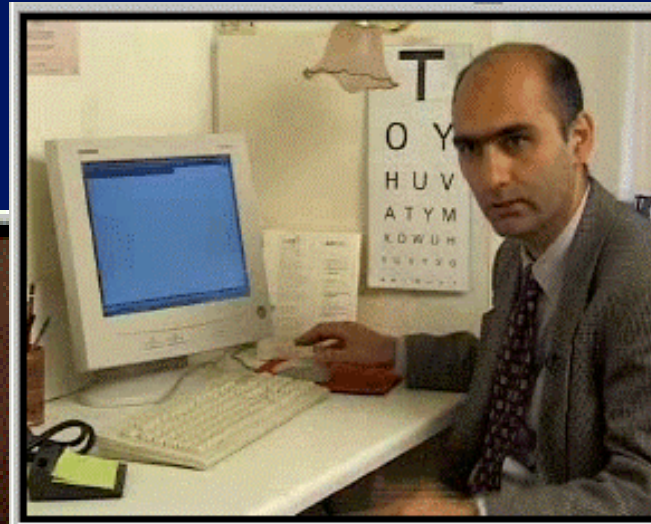
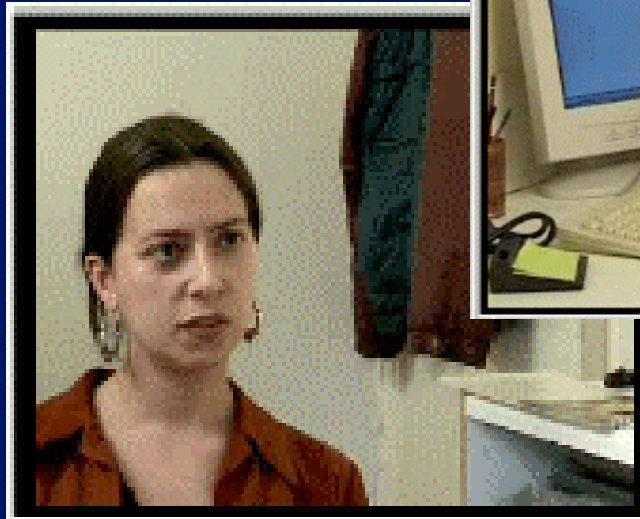
**General
Explanation**

**Referral
Advice**

**Reasons for
Advice**

Primary care referrals: ERA

Jon Bury, Michael Humber





To use ERA, you will need Microsoft Internet Explorer 5 or above ([get the latest version](#)).

ERA - Early Referrals Application

To make a referral click on "Electronic referral" under the appropriate heading ([ERA overview and tutorial](#))

Lung

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Breast

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Upper Gastrointestinal

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Colorectal

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Haematological

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Sarcoma

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Skin

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Neurological

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Gynaecological

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Head and Neck

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Urological

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Paediatric

- [Electronic referral](#)
- [Key points](#)
- [Referral guidelines](#)

Patient Details:

Age: Gender: M F

Referral information (please tick boxes):

Breast lumps:

Discrete lump Yes No
Asymmetrical nodularity persistent at review after menstruation Yes No
Abscess Yes No
Persistent / refilling cyst Yes No

Skin changes:

Nodule Yes No
Distortion Yes No
Ulceration Yes No

Pain:

Intractable pain Yes No

Nipple discharge / changes:

Discharge Yes No
Blood stained Yes No
Large volume (sufficient to stain clothes) Yes No
Bilateral Yes No
Eczema Yes No
Recent retraction or distortion (<3 mths) Yes No



ERA recommendations

These are made on the basis of the clinical features presented to the system; they are intended to aid, not replace, clinical judgement:

A 2-week referral may not be appropriate because none of the standard indications for a 2-week referral apply to this patient.

A referral to a breast specialist, though not necessarily urgent, would be appropriate

The following criteria apply to this patient:

- asymmetrical nodularity persistent at review after menstruation

[Explain](#)[Refer](#)[Quit](#)**Patient Details:**Age: Gender: M F 

Open source knowledge?

The image displays three overlapping windows of Microsoft Internet Explorer, each titled "Protocol Source - Microsoft Internet Explorer". The top window shows a rendered view of a PROforma guideline, while the bottom window shows the corresponding XML source code.

PROforma Guideline: Breast

- plan:**Breast**
- enquiry:**Clinical information**
- decision:**Referral decision**
- action:**No two week referral**
- action:**Two week referral**
- action:**Non urgent referral**

XML Source Code:

```
<!DOCTYPE decision (View Source for full doctype...)>
- <decision name="Referral_decision"
  choice_mode="single" support_mode="symbolic">
  <caption>'Referral decision'</caption>
  - <candidates>
  - <candidate name="Two_week_referral">
    - <arguments>
      - <argument support="for">
        <proforma_condition>
          ( tissue_changes includes
            'Discrete lump' and age >= 30 )
        </proforma_condition>
      </argument>
      - <argument support="for">
        <proforma_condition>
          ( skin_changes includes
            Ulceration )
        </proforma_condition>
      </argument>
      - <argument support="for">
        <proforma_condition>
          ( skin_changes includes
            Nodule )</proforma_condition>
      </argument>
      - <argument support="for">
        <proforma_condition>
          ( skin_changes includes
            Distortion )
        </proforma_condition>
```

Acute Lymphocytic Leukaemia

Jon Bury *with* ICRF Clinical Databases group *and*
The London Hospital Paediatric Oncology Unit

MRC ALL97 trial manager

Maintenance

(1) Trial database

Site:

Patient's name:

Date of birth: 23/05/1994

Age: 6

Arm: B

Steroid: Dexamethasone

Thiopurine: 6-Thioguanine

(2) Current status

Weight: Taken:

BSA: 0.8

Cycle: 2

Week: 55

Thiopurine dose: % mg

Methotrexate dose: % mg

(3) Results history

Previous cycle : 1

Date	29/02	06/03	13/03	20/03	27/03	03/04	10/04	17/04	24/04	01/05	08/05	15/05
Week	40	41	42	43	44	45	46	47	48	49	50	51
Hb	10.6	12.6	9.8	9.6	9.2	10.6	9.8	10.6	12.2	12.6	12.3	12.6
WCC	3.0	3.7	4.1	4.9	4.0	3.7	4.1	4.9	4.0	3.7	3.1	3.9
				2.3	1.9	2.3	1.9	2.3	1.9	1.5	1.9	1.3
				180	180	160	160	120	100	120	160	160

Overview of
patient status

New data
requested

Date	12/06		
Hb	12.6	10.8	10.6
WCC	3.7	4.1	4.9
N	1.6	1.8	2.4
Pts	160	160	120

New full blood count -

HB: WCC: Neutrophils: Pts:

(4) Suggested new dosagesOral Methotrexate % mg6-Thioguanine % mg

Reasoning:

Falling platelets. Doses should increase to 75% when platelets recover to over 75.

Guidance on treatment is
automatically generated

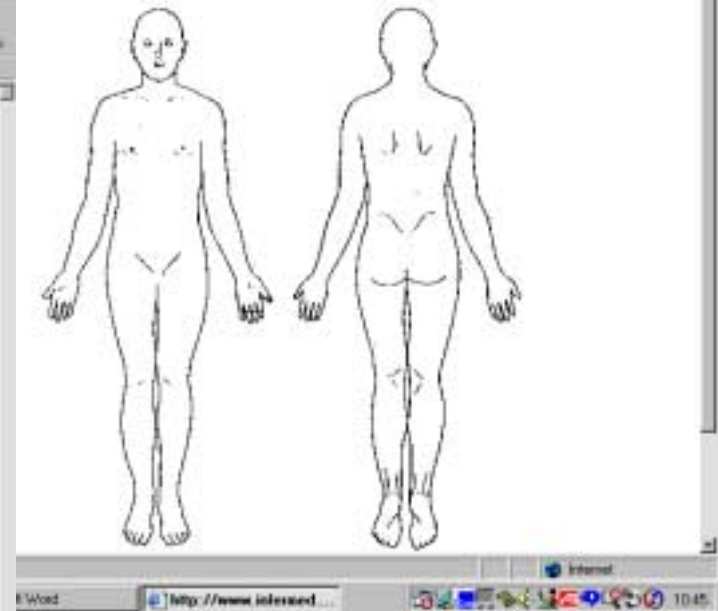
Palliative care: Arno



The screenshot shows the 'arno (with body chart)' application interface. It features a sidebar with a list of pain syndromes and a main content area displaying a decision tree for 'visceral_solid_organ_pain'. The sidebar includes the AREZZO logo and the following items:

- arno (with body chart)** Substituir nome
- pain syndrome decision**
- visceral_solid_organ_pain All selected
- visceral_solid_organ_pain
- superficial_somatic_pain
- deep_somatic_pain
- neuropathic_pain
- visceral_hollow_organ_pain

The main content area shows a decision tree for 'visceral_solid_organ_pain' with arguments for and against various options. A 'Continue' button is visible at the bottom of the sidebar.



demostudy - [demostudy schedule]

File View Options Communication Monitor References Reports Window Help

Study: demostudy Site: ICRF Subject: 1 Label: EG 1

demostudy - [eForm]

File View Options Communication Monitor References Reports Window Help

Study: demostudy Site: ICRF Subject: 1 Label: EG 1

MACRO

Visit: Screening visit Form: Exclusion Criteria

Navigation: First Return to Schedule Cancel

Question: mainauthorise

A positive screen for drugs of abuse at screening? No Yes ✓

Concomitant disease or condition that could, in the opinion of the investigator, increase the risk of adverse events? No Yes ✓

Prior administration of study therapy? No Yes ✓

If any box is marked yes, the patient will not be included in the trial

Will the subject participate in the study? No Yes ✓

Date of consent: 12/01/2000 ✓

If not participating, please give reason:

I certify that the data entered for this subject is correct and in accordance with our records. Certified ✓

This question needs to be answered by an individual with the following role: authoriser (Authoriser)

Validation: Audit Trail

Comments: Add Delete

Clear (F3)

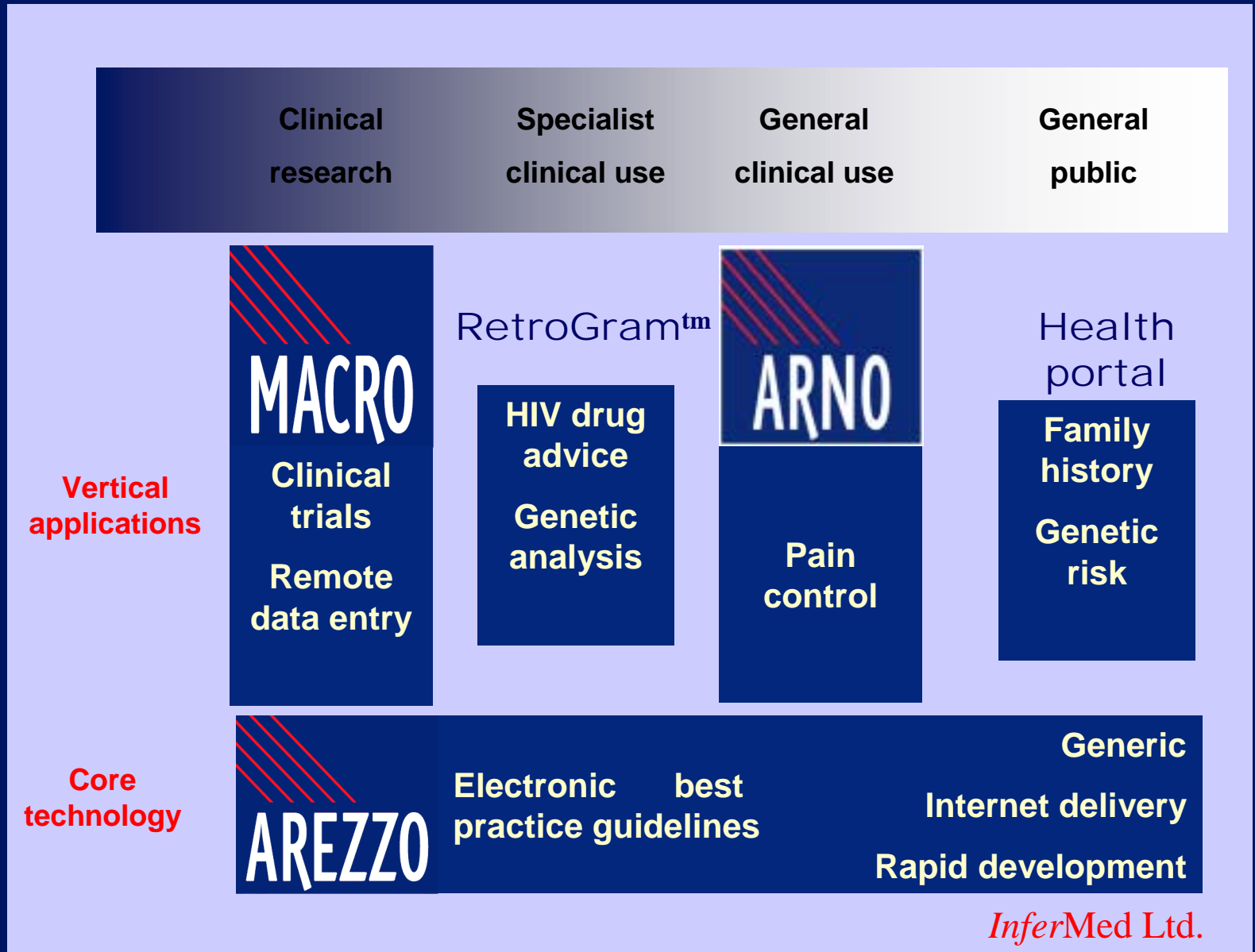
Reject if Warn if Inform if Comment OK Missing Unobtainable Not applicable

Logout Current User: rde (rde) Role: MacroUser 27/04/00 15:57 Function Keys Symbol

MACRO trial manager

InferMed Ltd.

Arezzo applications



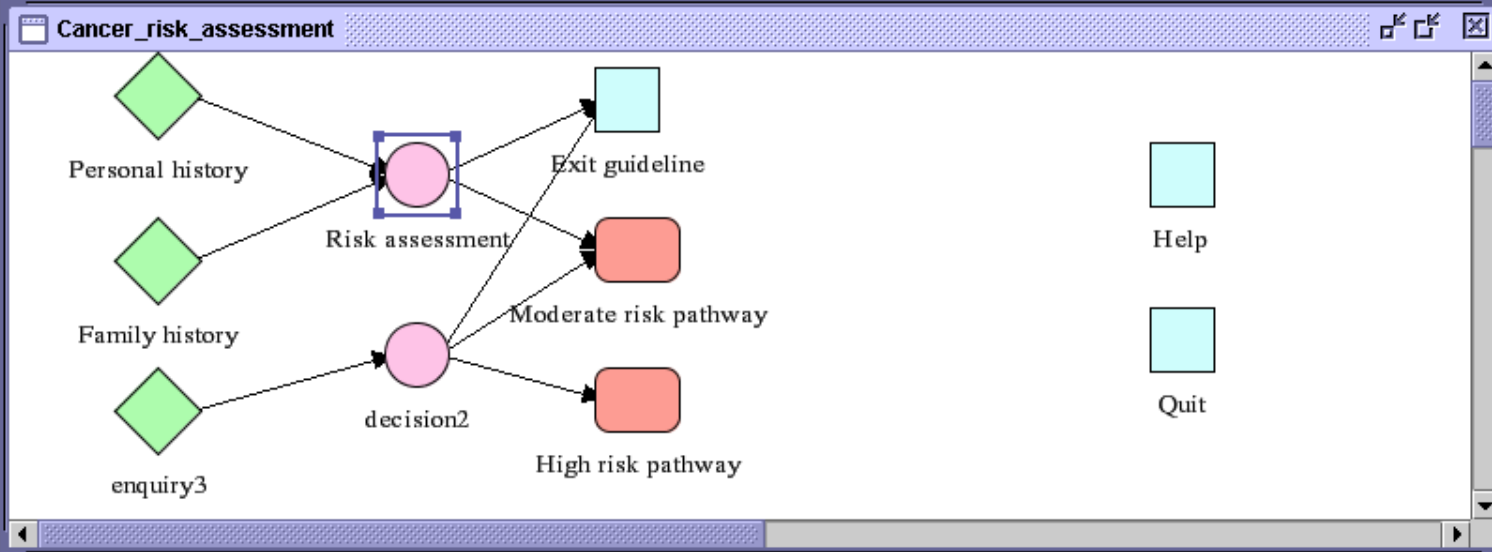
Current ICRF research

New research release

- Refined language syntax and semantics
- New Java toolset
 - Composer
 - Tester
 - Engine
 - Web server
- PROforma reference engine



- ◇ Personal history
- ◇ Family history
- ◇ enquiry3
- Risk assessment
- decision2
- Exit guideline
- Moderate risk pathway
 - ◇ Consent given
 - Do monitoring
 - Order screen
- High risk pathway
- Help
- Quit



PROforma	
Common Task Attributes	
Common Attrib	Proforma
Instance Name	Risk_assessment
Caption	Risk assessment
Description	
Parameters	
Goal	
Pre_Cond.	
Post_Cond.	
Trigger	
Cycle Until	
Cycle Repeat	
Cycle Number	1

Risk_assessment Decision Specific Attributes

Candidates Sources Arguments Decide Parameters

New Candidate

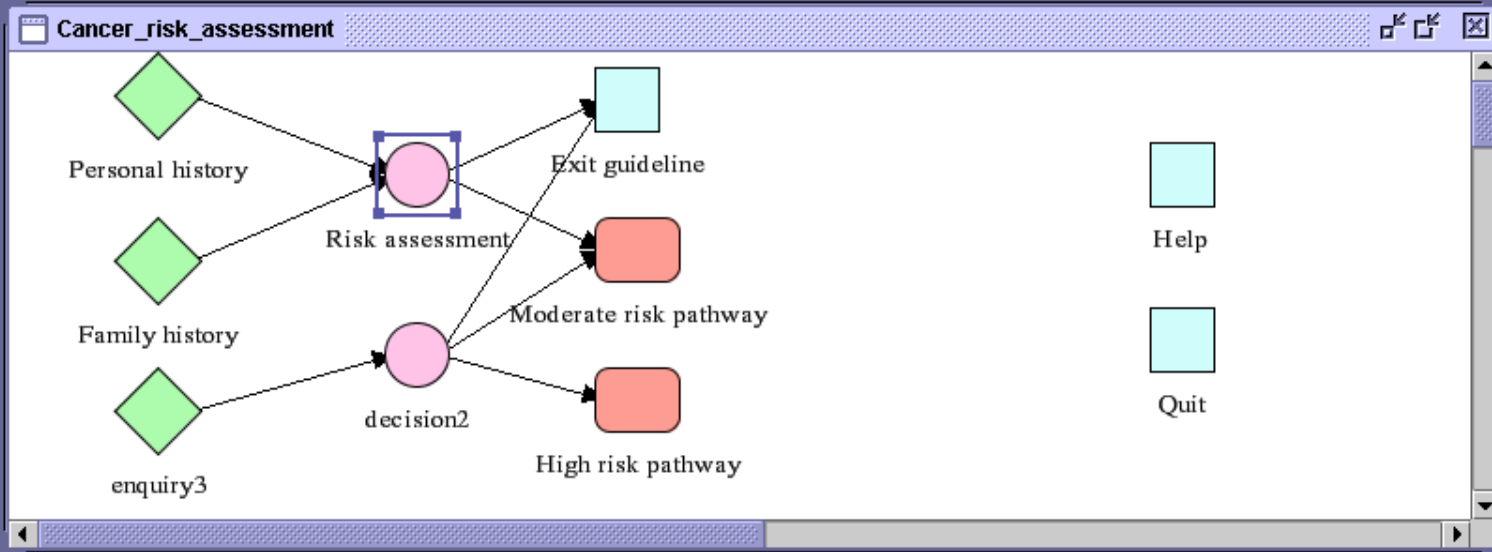
Priority

Candidate list

population	(0)
moderate	(0)
high	(0)



- Personal history
- Family history
- enquiry3
- Risk assessment
- decision2
- Exit guideline
- Moderate risk pathway
- Consent given
- Do monitoring
- Order screen
- High risk pathway
- Help
- Quit



PROforma Common Task Attributes

Common Attrib **Proforma**

```

decision :: Risk_assessment ;
caption :: 'Risk assessment' ;
choice_mode :: single ;
support_mode :: symbolic ;
candidate :: high ;
    recommendation :: Netsupport( Risk_assessment, high) >= 1 ;
candidate :: moderate ;
    recommendation :: Netsupport( Risk_assessment, moderate) >= 1 ;
candidate :: population ;
    recommendation :: Netsupport( Risk_assessment, population) >= 1 ;
end decision .
  
```

Risk_assessment Decision Specific Attributes

Candidates **Sources** **Arguments** **Decide** **Parameters**

New Candidate

Priority

Candidate list

population	(0)
moderate	(0)
high	(0)

REACT care planner

David Glasspool,
Tito Castillo
Vicky Monaghan

The screenshot displays the REACT care planner interface. At the top, there is a menu bar (File, Edit, View, Domain, PROforma) and a toolbar with icons for Open, Save, Cut, Copy, Paste, Print, and Help. The 'Domain' is set to 'Breast cancer'. Below the menu is a 'Plan' section with tabs for Plan 1, Plan 2, and Plan 3. A list of interventions is shown on the left, including pregnancy, breastfeeding, self examination, mammographic screening, tamoxifen, bilateral mastectomy, and oophorectomy. The main area shows a timeline from age 20 to 60. Colored bars represent the duration of each intervention: pregnancy (red), breastfeeding (blue), self examination (green), mammographic screening (green), tamoxifen (green, starting at age 32), bilateral mastectomy (blue), and oophorectomy (blue). A red bar at the bottom right indicates a 2% risk. Below the timeline is a table with columns for Risk and Cost. At the bottom, there are tabs for Recommendations, Review Arguments, and Scenarios. The 'Review Arguments' tab is active, showing a decision tree for 'Decision to start tamoxifen at 32'. The tree includes arguments for and against starting tamoxifen, such as 'There are good reasons to act to reduce risk' and 'There are a number of reasons to consider not starting Tamoxifen'.

REACT
Help

File Edit View Domain PROforma

Open Save Cut Copy Paste Print Help Domain Breast cancer

Plan 1 Plan 2 Plan 3

Delete

Edit Domain

Clear

History

Plan

pregnancy

breastfeeding

self examination

mammographic screening

tamoxifen

bilateral mastectomy

oophorectomy

Now aged 30

20 30 40 50 60

Risk Cost ...

2%

Recommendations Review Arguments Scenarios

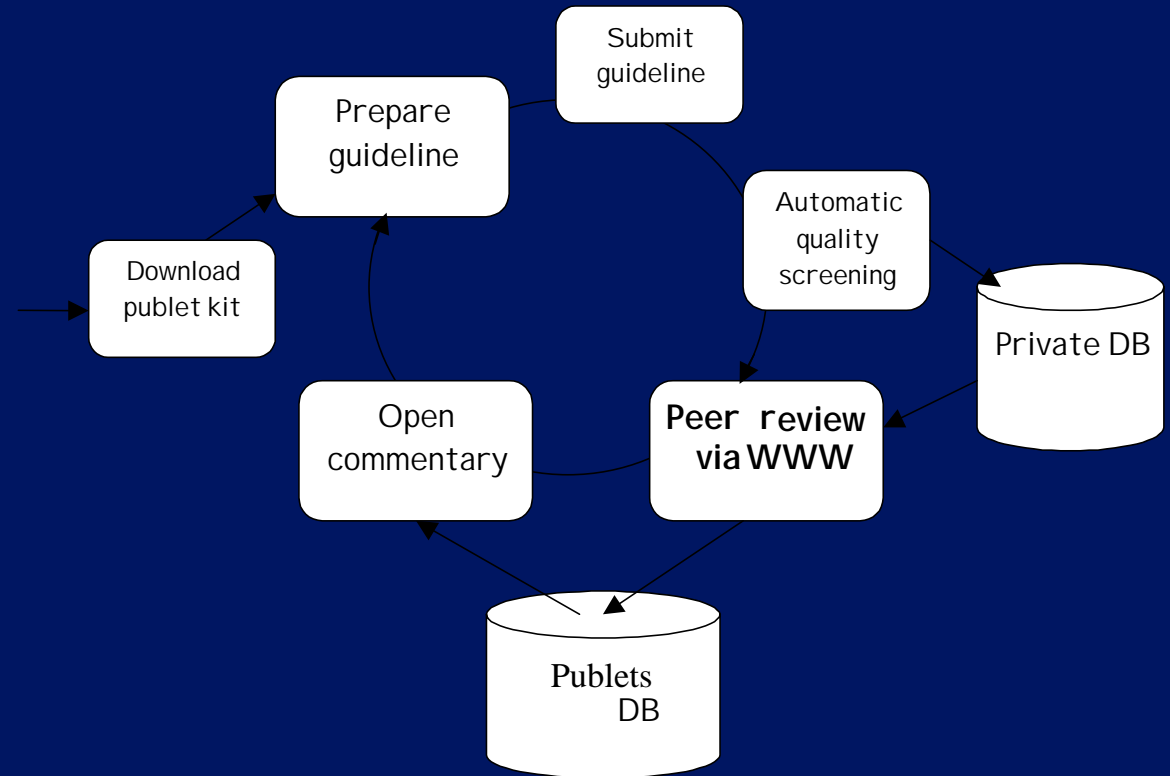
Decision to start tamoxifen at 32

- There are good reasons to act to reduce risk
- There are a number of reasons to start Tamoxifen
 - Tamoxifen has major benefits for women who have had surgery for breast cancer
 - REASON: reduces recurrence by more than a third (43%)
 - REASON: reduces deaths by nearly a quarter (22%)
 - REASON: reduces cancer in other breast by nearly a half (47%)
 - By analogy Tamoxifen may work to prevent breast cancer in a healthy at-risk woman
- There are a number of incidental health benefits
- There are a number of reasons to consider not starting Tamoxifen
 - Side effects: Hot flushes, vaginal bleeding, secretions
 - Increased risk of endometrial cancer
 - BUT: Mainly post-menopausal
 - BUT: rare (1 in 10,000 per annum rises to 6-9 in 10,000 p.a.)
 - BUT: treatable (hysterectomy) if symptoms are reported
 - Risk of blood clots
 - Risk of eye problems

“Publet” technology

Ali Rahmanzadeh

David Sutton



Updated and expanded every six months

CE

SOLO Application Launcher

Protocol Servers

- Sample_Server
 - signbreastcancer
 - Jasmin Chew
 - Jan Baker
 - bowel
 - breastcancer
 - depression
 - dyspepsia
 - asthma
 - healthydiet
 - ibs
 - Mamogram

Jasmin Chew, Female, age 28

Confirm Data

Restart

Stop

Patient Medical | Guidance

Patient Medical

Age? 26

Lump?
 Yes
 No

Pain?
 Yes
 No

Nipple Discharge?
 Yes
 No

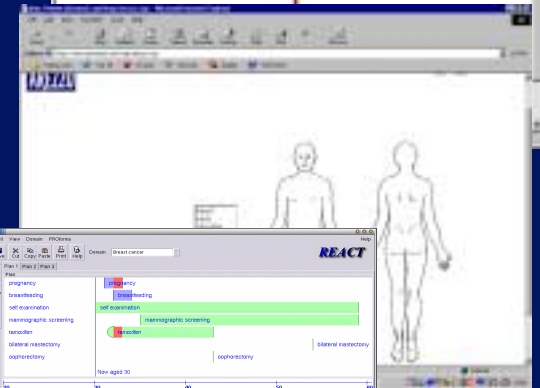
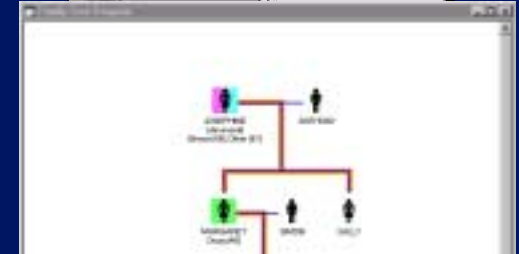
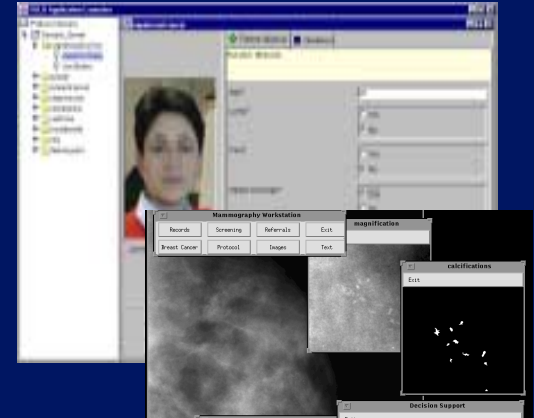
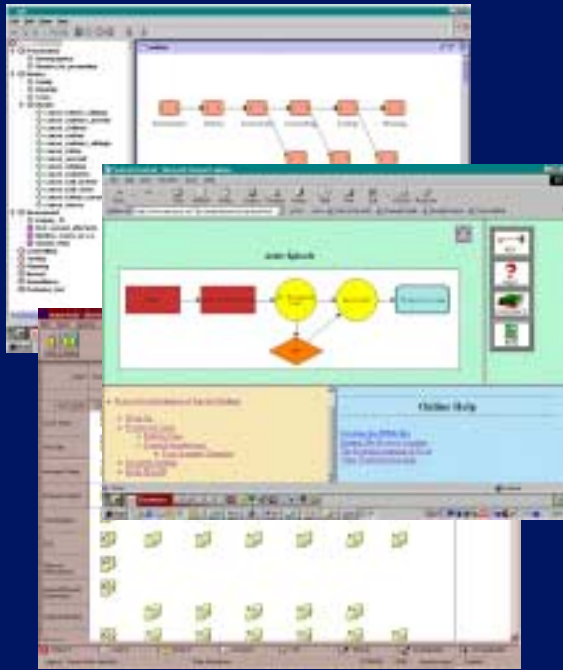
Nipple Retraction or Distortion, Nipple Eczema?
 Yes
 No

Change in Skin Contour?
 Yes
 No

The name of the guideline under TEST is :
BMJ_Cardiology_1_Dr._J_Fistein_V1.0.az

Cancel

OpenClinical server



Protocol &
guideline
databases

