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Decision support for health care: the PRO*forma* evidence base

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ABSTRACT

Cancer Research UK has developed PRO*forma*, a formal language for modelling clinical processes, along with associated tools for creating decision support, care planning, clinical workflow management and other applications. The PRO*forma* method has been evaluated in a variety of settings: in primary health care (prescribing, referral of suspected cancer patients, genetic risk assessment) and in specialist care of patients with breast cancer, leukaemia, HIV infection and other conditions. About nine years of experience have been gained with PRO*forma* technologies. Seven trials of decision support applications have been published or are in preparation. Each of these has shown significant positive effects on a variety of measures of quality and/or outcomes of care. This paper reviews the evidence base for the clinical effectiveness of these PRO*forma* applications, and previews the CREDO project – a multi-centre trial of a complex PRO*forma* application for supporting integrated breast cancer care across primary and secondary care settings.

Keywords: clinical guidelines, computer-interpretable guidelines, decision support, e-health

PRO*forma*: modelling decisions and care pathways

PRO*forma* is a formal language for describing guidelines, care pathways and protocols, and for automating clinical processes.[1,2] The method is mathematically principled and designed to be intuitive to clinicians. The former supports reliable and sound applications; the latter empowers clinicians to oversee the development of clinical applications and their safe use in practice – neither of which are typical of conventional software. Application development tools include the Arezzo® system available from *Infer*Med Ltd,[3] and the Tallis system which is used at Cancer Research UK (CRUK) for internal and collaborative research projects.

PROforma: the evidence base

The PRO*forma* approach has led to several novel technologies, and a body of evidence gained from a range of settings shows that they could have substantial clinical value.

The first practical application of PRO*forma* was CAPSULE, a system for assisting general practitioners in prescribing for common conditions.[4] Prescribing is an important application for decision support in many clinical areas, because it requires clinicians to be able to access a large amount of constantly changing knowledge in order to stay up to date. CAPSULE took in patient data and produced a short list of relevant medications, together with the arguments for and against each option. Walton *et al*'s trial of the system showed potential substantial improvements in quality of prescribing (about 30%, $P<0.001$), improved resource use and faster decision making.

Prescribing tools also have a role in cancer care. LISA is a PRO*forma* system for advising on dose adjustment in the treatment of children with acute lymphoblastic leukaemia. A first trial of the system[5,6] showed that without decision support, clinicians non-deliberately deviated from the trial protocol on 22.9% of occasions. With decision support this figure dropped

to zero. Of the clinicians involved, 32 out of 36 (almost 90%) said they would use LISA if it were routinely available. (Note that the results of this LISA trial are indicative rather than definitive since the trial was run on retrospective cases.) LISA has now been incorporated into *Infer*Med's MACRO® clinical trial manager, which is being prospectively evaluated in a clinical trial led by Cancer Research UK's Paediatric Oncology Unit at the London Hospital.

Definitive results have been published for an important class of application designed to tailor drug selection and dose according to virus genotype mutation data. Complex genotype data are being increasingly used in clinical decision making, providing a significant opportunity for computerised decision support to handle and interpret them effectively. The RetroGram® system[7] is a PRO*forma* application, developed by *Infer*Med for Hoffman la Roche, which advises on the use of anti-retroviral therapy for HIV-positive patients, based on HIV-1 genotype information. It is in use by more than 250 clinicians worldwide. The multi-centre Havana trial[8] showed that availability of genotype data, allied with RetroGram′s interpretation of those data and prescribing advice, significantly improved virological outcomes in patients (by around 33%), compared with conventional management of HIV-positive patients without genotype data.

Genetic profiling is becoming increasingly important in patient care generally, and could well be an important model for the future. However, individualised care in this area is difficult and time-consuming to plan, and very difficult to implement. PRO*forma* can support both phases, as illustrated by the REACT treatment planner,[9] a system based on PRO*forma* concepts. REACT was first demonstrated in the management of type 2 diabetes,[10] and has been trialled more recently in an application to assist in individualised care planning in a genetic counselling setting. This trial (as yet unpublished) has produced encouraging results: six out of eight clinical geneticists who used the system during counselling were supportive of its value. The approach adopted could be helpful in other care planning settings such as the management of chronic conditions and particularly in post-genomic medicine. As genetics and genomics acquire increased clinical significance and clinicians face growing demands to keep up to date with the science and increasing mathematical skills, decision support and care planning tools will become critical to achieving best standards of practice.

The problem of assessing genetic predispositions to cancer and other diseases further illustrates these issues. Genes predisposing to cancer attract considerable medical and public concern. As more genetic markers become available, individuals who are worried that they might be at risk seek guidance from their GPs and others. We know that GPs are willing to provide advice and support, but they often feel they do not have the expertise to take or analyse a family history. Further, the problem of communicating risk to patients who have no statistical understanding is notoriously difficult. The RAGs system was developed to help GPs take a family history, assess risk and explain risk factors to patients.[11] An application covering breast and ovarian cancer risk was implemented for collaborators in Oxford. Trials there showed that GPs produce significantly more accurate family trees, risk assessments and referral decisions with customised technologies such as RAGs than with paper and pencil or with statistical software such as Cyrillic.[12] In a comparison with statistical software and paper and pencil, RAGs was chosen as the preferred tool 91.7% of the time.

The CADMIUM imaging system used an early version of the PRO*forma* approach to combine conventional image processing with automated interpretation of images and diagnosis.[13] CADMIUM was trialled in a study in which radiographers with specialist training interpreted screening mammograms both with and without decision support. The trial was designed to highlight whether such systems could play a role in improving decision making in routine breast cancer screening. The system was designed to automatically identify microcalcifications in breast tissue and interpret the pattern of calcifications according to whether they were likely to indicate benign or malignant abnormalities. The study indicated that the system significantly increased the rate of correct classifications of malignant and benign abnormalities by radiographers, while also reducing cancer misses and false positives.

The most recent trial of PRO*forma* (as a module of the CREDO system described in the next section) was also in breast cancer. The study looked at the value of decision support in the initial assessment ('Triple Assessment') of women referred to specialist breast clinics. A collaborating breast surgeon used PRO*forma* to formalise national guidelines for genetic risk assessment and for decisions about imaging (mammography and ultrasound), biopsy and management. The trial involved a random sample of 24 doctors working as consultants or registrars in specialist breast units with, on average, nine years' experience. They were asked to 'manage' ten paper cases, five with and five without decision support, and their decisions were compared with a consensus of best practice defined by an expert panel. Without support, decisions deviated from the consensus standard in approximately 50% of cases; with support, this figure dropped to 16%. The majority of deviations were minor, but when decision support was not available, 8.3 % of decisions were judged to represent critical errors with potential for patient harm. This figure fell to 0.8% when decision support was provided.

To summarise, of seven studies of PRO*forma* applications that have yielded quantitative data, all have

shown significant positive results on a variety of outcome measures. With the simplest assumption that the results were equally likely to go either way, this pattern has a chance probability of less than 0.01 ($0.5^7 = 0.008$).

The CREDO trial

With the exception of the RetroGram study, trials of PRO*forma* concepts and tools carried out to date have been undertaken under controlled research conditions rather than in routine clinical settings. The next planned trial of a PRO*forma* system will be the largest to date and is designed to redress the balance. The CREDO trial will focus on breast cancer care and will seek definitive data on the value of advanced tools for decision support, care planning and multidisciplinary care throughout the patient journey. CREDO is designed to support seamless patient management across primary and secondary care sectors, from presentation and diagnosis through to treatment and follow-up.

The CREDO system is based on a comprehensive service model that maps the entire breast cancer care pathway in a form that lends itself to computerisation.

The CREDO service model (see Figure 1) suggests that across the whole breast cancer journey there are over 220 services delivered by different professionals in secondary and primary care settings. It further suggests that there are approximately 65 decision points where there is potential for errors that could significantly impact on treatment efficacy or patient safety. It is interesting to note that on a simple probability model, if error rates are limited to 1% across the 65 decisions, only 50% of women, on average, will get perfect care. If error rates are raised to 5%, only 3% of women will get perfect care. Evidence from various studies and reports, such as Vincent's work in National Health Service (NHS) acute hospitals,[14,15] suggests that actual rates of deviation from evidence-based recommendations could be 10% or higher. A main goal of the CREDO trial is to determine to what extent a reduction in error rates is achievable in practice through the use of decision support.

Improving the interface between primary and secondary care

One of the aims of CREDO is to improve communications between clinicians, and shared care of patients undergoing cancer care. The 2001 joint report by the Commission for Healthcare Improvement (now the Healthcare Commission) and the Audit Commission on cancer care[16] found that cancer care is often fragmented, and that problems arise at the interfaces where information and responsibilities are transferred between care sectors. Inadequate co-ordination between primary care (where initial detection, primary risk assessment and sometimes follow-up of a cancer occurs) and secondary care (where most of the treatment takes place) can increase patients' feelings of uncertainty. One of the reasons for this is that GPs and breast specialists have different roles and view the process from different perspectives. However, from the patient's point of view, the entire process, from her first visit to the GP through to follow-up, is a single journey.

CREDO aims to enhance shared care by acknowledging the different goals and roles of the different stakeholders (primary and secondary care clinicians,

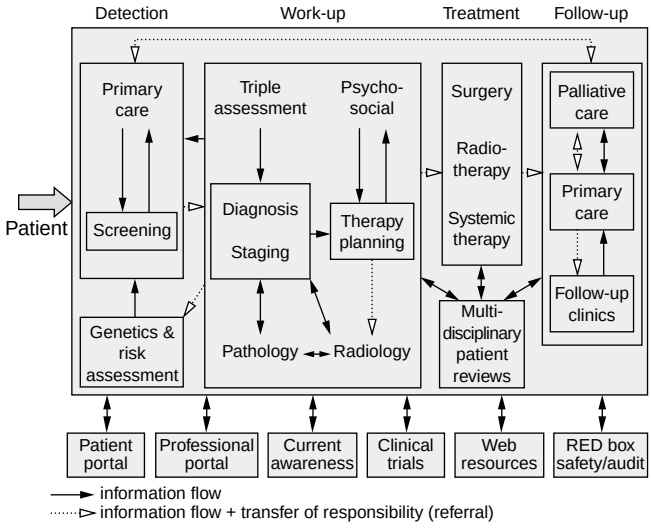

Figure 1 CREDO service model

nurses, patients ...) involved in a complex pathway. The system allows them to access the same underlying evidence-based computerised care process, but provides different representations of it to meet their different needs. For example, CREDO provides a simple and intuitive visual family tree for GPs to facilitate familial breast cancer risk assessment and communication of genetic relationships (see Figure 2). Based on the patient's risk category (population, moderately elevated or high risk), CREDO can also suggest appropriate management or referral to specialists if needed.

For women with medium and high risk, family history information can be passed automatically to the appropriate specialist in secondary care. A CREDO module (based on REACT, see Figure 3) can then help gather further objective and subjective patient data in order to generate risk or other graphs, together with the pros and cons of alternative pre-emptive interventions.

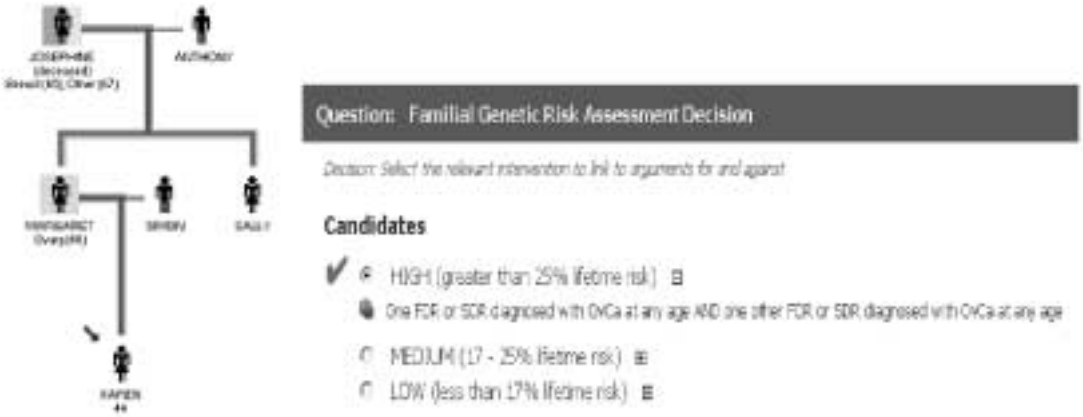

Figure 2 CREDO style of family history taking and risk assessment (based on the RAGs system developed by Coulson *et al*, 2001[11])

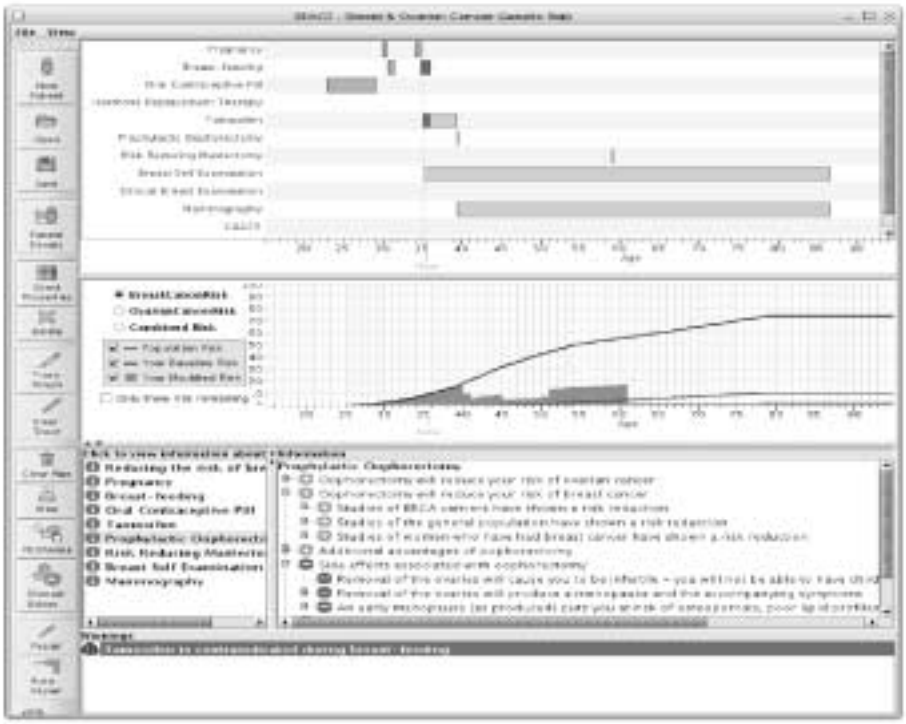

Figure 3 The REACT application for planning the care of women with elevated breast cancer risk. The top window shows a personalised plan of interventions over time; the central window shows the risk curves associated with the plan and the arguments for and against each intervention. The bottom window provides any significant alerts or reminders associated with the plan

CREDO is intended to support the increasingly demanding routines and individualised care plans ('workflows') that are required as cancer care becomes more complex, thereby reducing the clinician's administrative burden and facilitating good communication between the many individuals and specialties involved in the patient's care.

Special emphasis is being given to automating information exchange between hospital and primary care settings to keep GPs informed about their patients' treatment status, and facilitate their participation in management and follow-up activities. There is some evidence in the literature to suggest that follow-up in primary care settings is acceptable to patients and provides similar outcomes to specialist follow-up in breast cancer,[17] but the higher demands on practitioners will presumably only be acceptable if these are offset by automated communication, record keeping and other benefits of computerisation.

Overall, the CREDO trial will seek to address the following questions:

1 Can PRO*forma*-based decision support help bring about improved consistency, quality and safety in clinical decision making and patient management throughout the patient journey?
2 Can the services be offered in a form that is acceptable to and valued by clinicians?
3 Can an integrated care pathway such as CREDO also help to manage the administrative requirements of complex pathways and, through automation, lead to reduced administrative load for clinicians?
4 Can the system help improve the experience for the cancer patient?

We have successfully constructed a prototype of a decision support and workflow management system for breast cancer in collaboration with clinical colleagues at Guy's Hospital (London, UK) and Addenbrookes Hospital (Cambridge, UK). We believe that this demonstrates that it is feasible to build a system to support clinical decision making for many of the 65 decisions iden-tified in the care pathways for women with (or at risk of developing) breast cancer, and provide support in an intuitive and clinically acceptable way. A website for the CREDO trial is under construction but an early demonstration version is available.[18]

Conclusion

This paper has summarised the evidence base for the clinical value of guideline-based decision support applications implemented using the PRO*forma* method. While the majority of the evaluation studies carried out to date (with one significant exception) have been undertaken in 'laboratory' conditions, all have produced positive results. These have led us to initiate the CREDO project: a multi-centre trial, covering primary and secondary care settings, of a complex application for supporting integrated breast cancer care. This trial is expected to yield definitive results on the clinical effectiveness of PRO*forma*-based technologies and applications. Comments, suggestions and questions are welcome and can be addressed to credoinfo@acl.icnet.uk.

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CONFLICTS OF INTEREST

None.

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