PROforma guidelines and care pathways: summary of the approach and results of trials

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Background

“There have been undoubted improvements in service delivery but there is still a sense that progress has been patchy and that much has yet to be achieved.”

As demands for more and better patient care continue to grow the shortcomings of medical services are increasingly recognized. To Err is Human, an influential report from the US Institute of Medicine (Kohn et al, 1999) focused attention on human factors in achieving consistently safe decision-making in difficult conditions. Quality and safety are now major issues with many governments and agencies pursuing policies to improve care at both individual and organizational levels. In the UK the difficulties for hard-pressed clinicians to deliver consistently high quality, safe care are also increasingly well documented. In cancer services, the joint report by the Commission for Healthcare Improvement and Audit Commission on cancer care identifies a wide range of challenges to the consistent delivery of effective detection, diagnosis and treatment.

In a series of publications over the last 15 years staff of CRUK’s Advanced Computation Laboratory have also argued that human factors have major implications for efficacy and safety of care and that a new class of computer systems capable of decision-making and care planning have an important contribution to make. Such technologies are now seen as a key resource in the delivery of modern, evidence-based clinical services. The UK Government has committed £6.7 billion over 6 years as part of its modernization program for the NHS through the National Programme for IT (NpfIT).

PROforma: modeling pathways and protocols

CRUK’s approach to this problem is unusual in being grounded in formal computer science and cognitive science (see ACL quinquennial report, November 2004). The approach has led to several novel technologies and a body of evidence that they may have substantial clinical value in a range of settings, which is summarized in the next section. The pivot of ACL research

1 www.openclinical.org
2 Vincent et al and other sources www.openclinical.org
5 Figures and timescales vary across sources but it is generally agreed that “The National Programme for IT represents an unprecedented level of central investment in information systems within the NHS and a significant opportunity for … improving and modernising services”.
is PROforma, a formal language for describing guidelines, care pathways and protocols and automating clinical processes (Fox and Das 2000; Sutton and Fox 2002). PROforma is mathematically principled while still being intuitive to clinicians. The former means reliable and safe applications, the latter means clinicians are empowered to oversee clinical development and use – neither of which are typical of conventional software.

Peleg et al (2002) and de Clercq et al (2004) have carried out independent comparisons of published approaches to modelling guidelines and protocols noting that PROforma was the first of a family of proposals in this area and seems to be best established in clinical use (Peleg, pers comm.). It is the only one with proven theoretical foundations and a comprehensive set of practical application development tools (de Clercq et al 2004). The ACL has developed several generations of such tools, including the Arezzo® system licensed to InferMed Ltd and the Tallis system which is used for internal and collaborative research projects. The PROforma research programme was identified as “outstanding” in CRUK’s quinquennial review of the ACL.

**PROforma: evidence base**

The first practical application of PROforma was CAPSULE, a system for assisting general practitioners in prescribing for common conditions. Prescribing is an important application for decision support in many clinical areas, because of the amount of knowledge clinicians must absorb to stay up to date. Although a pilot trial of CAPSULE showed dramatic potential improvements in decision quality (about 30%) and in resource use and faster decision-making (Walton et al, BMJ 1997) it was not possible to follow this up in a full trial as a system called Prodigy was adopted as the NHS standard about this time. Prodigy became the focus of NHS investment for some years and remained the preferred prescribing aid until 2003 when it was apparently abandoned.

Prescribing tools also have a role in cancer care. LISA is a PROforma system for advising on dose adjustment in treatment of children with acute lymphoblastic leukaemia. LISA is incorporated into a clinical trial lead by CRUK’s Paediatric Oncology Unit at the London Hospital and now integrated into InferMed’s MACRO® clinical trial manager. The first full trial shows that without decision support clinicians deviated from the trial protocol on 37% of occasions but with support this dropped to zero. 35/36 of the clinicians said they would use LISA if it were routinely available (Bury et al, 2004 a,b). Note

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6 In 1996 the development team was awarded the 20th Anniversary Gold Medal and Laureate Prize of the European Federation of Medical Informatics for its development.

7 [www.infermed.com](http://www.infermed.com)
that this trial is only indicative rather than definitive since it was run on retrospective cases; prospective trial results should be available in 2005.

Definitive results are available, however, for a very important class of applications in tailoring drug selection and dose to individual patient profiles. The Retrogram® system is a PROforma application developed by InferMed for Hoffman la Roche. Retrogram advises on the use of anti-retroviral therapy for HIV+ patients and is understood to be in use with more than 250 clinicians worldwide. The HAVANA multicentre trial (Tural, AIDS 2002) has shown that availability of genotype information significantly improves clinicians’ decision-making as measured by viral load, but with Retrogram providing genotype interpretation and decision support services one third more patients’ viral loads were reduced to the target level.

As genetic profiling becomes increasingly important in cancer care this could well be an important model for the future. However, individualised care is difficult and time-consuming to plan, and very difficult for busy clinical teams to implement (many tired professionals might say impossible). PROforma can facilitate both steps. An example is a treatment planner for patients with type 2 diabetes and hypertension (see video at www.openclinical.org). A trial of the system to assist in individualized care planning in a genetic counseling setting has produced very encouraging results, with 7/8 clinical geneticists being strongly supportive of its value. This approach could be helpful in cancer management generally, chemotherapy and radiotherapy planning for example, and in the multidisciplinary meeting.

Genetics is an important area where clinicians will increasingly need support, due to the demands of keeping up to date with the science and mathematical skills required. The problem of assessing genetic pre-dispositions to cancer and other diseases illustrates this. Genes predisposing to cancer attract considerable medical and public concern. As more genetic markers become available, individuals who are worried they are at risk seek guidance from their GPs and others. We know that GPs are willing to provide advice and support, but they do not generally feel they have the expertise to take or analyse a family history, and the problem of communicating risk to patients without statistical understanding is notoriously difficult. RAGs was

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8 InferMed has also developed PROSPECT, which provides evidence-based (Cochrane) and procedure-specific recommendations and decision support for the management of postoperative pain in commonly performed surgical procedures (see www.postoppain.org) and ORAMA for management of renal anaemia which combines PROforma decision support with the MACRO clinical trial manager and electronic data capture system (see http://www.infermed.com/news-items/2004-05-28). CRUK and InferMed have also collaborated successfully on ERA, a system for advising GPs on early referral of suspected cancers (http://www.infermed.com/era) and Clinical Evidence Interactive, with BMJ Publishing. While technically successful these projects have not as yet led to clinical trials or refereed publications and so are excluded from this summary.
developed to help the GP take the family history, assess risk and explain risk factors to patients (Coulson et al, 2000). An application for breast and ovarian cancer risk was implemented for collaborators in Oxford and trials there showed that GPs produce more accurate family trees, risk assessments and referral decisions than with paper and pencil (Emery et al, 2000). In a comparison with Cyrillic (a leading pedigree drawing and risk assessment package aimed at geneticists) RAGs was chosen as the preferred tool 91.7% of the time, as opposed to 5.6 % for Cyrillic and 2.7% for pen-and-paper techniques. 

The CADMIUM imaging system used an early version of the PROforma approach to combine conventional image processing with automated interpretation of images and diagnosis. CADMIUM was trialled in a study in which radiographers with specialist training interpreted screening mammograms with and without decision support. The question was whether such systems could play a role in, or even substitute for consultant radiologists, in routine breast cancer screening. The system was designed to identify micro-calcifications in breast tissue automatically and interpret the pattern of calcifications in terms of whether they are 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 while also reducing cancer misses and false positives (Taylor et al; 1999).

The most recent trial of PROforma is also in breast cancer, looking at the value of decision support in the initial assessment of women referred to specialist breast clinics. PROforma was used to formalise national guidelines for genetic risk assessment and for decisions about imaging (mammography and ultrasound), biopsy and management. A random sample of 24 doctors, working as consultants or registrars in specialist breast units (average 9 years experience) “managed” 10 paper cases, 5 with and 5 without decision support and their decisions were compared with the consensus of best practice developed by an expert panel. Without support decisions deviated from the consensus standard on approximately 50% of cases, but with support this dropped to 16%. The majority of these deviations were minor but 8.3 % were judged as representing critical errors with potential for patient harm when decision support was not available, and this fell to 0.8% when it was provided (Hurt, Patkar et al, in preparation).

To summarise, in the seven studies to date of PROforma decision support and related applications that have yielded quantitative outcome data, all seven have shown strongly positive results on a variety of outcome measures.
Although there is some room for caution in interpreting these results the pattern appears to be highly significant (p < 0.01) and justifies considerable confidence that such technologies can have a major beneficial impact on quality and safety of care.

References

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