Urological cancer care pathways: development and use in the context of systematic reviews and clinical practice guidelines

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Abstract

Background Making healthcare treatment decisions is a complex process involving a broad stakeholder base including patients, their families, health professionals, clinical practice guideline developers and funders of healthcare.

Methods This paper presents a review of a methodology for the development of urological cancer care pathways (UCAN care pathways), which reflects an appreciation of this broad stakeholder base. The methods section includes an overview of the steps in the development of the UCAN care pathways and engagement with clinical content experts and patient groups.

Results The development process is outlined, the uses of the urological cancer care pathways discussed and the implications for clinical practice highlighted. The full set of UCAN care pathways is published in this paper. These include care pathways on localised prostate cancer, locally advanced prostate cancer, metastatic prostate cancer, hormone-resistant prostate cancer, localised renal cell cancer, advanced renal cell cancer, testicular cancer, penile cancer, muscle invasive and metastatic bladder cancer and non-muscle invasive bladder cancer.

Conclusion The process provides a useful framework for improving urological cancer care through evidence synthesis, research prioritisation, stakeholder involvement and international collaboration. Although the focus of this work is urological cancers, the methodology can be applied to all aspects of urology and is transferable to other clinical specialties.

The members of the UCAN Care Pathway Development Group are given in the “[Appendix](#)”.

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Introduction

Challenges in urological cancer treatment decision-making

In making healthcare decisions regarding treatment, decision makers are confronted with several fundamental issues. At the individual level, patients and clinicians are primarily concerned with the balance between the perceived benefits and harms of treatment discussed, whilst for healthcare systems, policy makers need to know which treatments should be provided. This societal aspect will be informed by information on costs, cost-effectiveness and arguably, some notion of fairness such as equal access for equal need. In conditions such as localised prostate cancer for which multiple management options exist, the situation becomes even more complex. One approach to facilitate individual decision-making and decisions regarding treatment provision

is evidence-based medicine [1], in which choices are made on the basis of the best available evidence obtained from robust methodology; evidence that is valid, reliable and of high quality. To be useful, this evidence must be readily accessible. Systematic reviews are one method of identifying and synthesising research evidence on a particular subject [2]. The review process, review findings and subsequent guideline recommendations can also be used to identify gaps in knowledge about treatment effects (uncertainties) and inform future work to address important gaps.

The strengths and limitations of systematic review methodology

Reasons for undertaking a systematic review include resolution of conflicting evidence or clinical uncertainties, explanation of variations in practice, or to confirm the appropriateness of current practice. To achieve these outcomes, a systematic review requires a transparent and replicable synthesis process [3] with effect estimates obtained by meta-analysis using appropriate statistical techniques.

Fig. 1 Localised prostate cancer care pathway. Abbreviations: PSA prostate-specific antigen, EBRT electron beam radiotherapy, IMRT intensity-modulated radiation therapy, HRPc hormone refractory prostate cancer, LHRH luteinizing hormone-releasing hormone, DXT

deep X-ray therapy, TURP transurethral resection of the prostate, GVAX granulocyte-macrophage colony-stimulating factor [or GM-CSF] vaccine, ZD4054 Zibotentan

Fig. 2 Locally advanced prostate cancer care pathway. For abbreviations, refer Fig. 1

Typically, a systematic review involves a well-formulated question or questions, comprehensive searches of the major electronic databases, pre-defined study eligibility criteria, an unbiased study selection process and data extraction against a set of pre-determined outcomes using standard forms. These data are critically appraised, including rating of the quality of the evidence and quantitative synthesis with meta-analysis where appropriate. This transparent and replicable process differentiates systematic from narrative reviews, which are more prone to bias.

A key limitation of any systematic review is that it cannot overcome problems inherent in the design, conduct and reporting of the included primary studies [3–5]. Their authority can also be undermined by errors in review methodology or reporting leading to variation in conclusions drawn by separate systematic reviews attempting to answer the same question. As a consequence, widely accepted guidelines for the conduct and reporting of primary studies and systematic reviews, such as CONSORT, Cochrane Handbook and PRISMA, [6–8] have been established.

Defining the question

Defining the review question for a systematic review is the first and most important stage of the process as this provides the direction for all subsequent stages [9]. Paradoxically,

while methodology has advanced for the actual process of a systematic review, there has been little work done to establish the best way of identifying areas of clinical uncertainty and prioritising a list of questions that maintains relevance for all interested groups. One approach is to perform a scoping study [10]; this involves an initial literature search to assess whether a full systematic review is both feasible, that is there are sufficient primary studies available for synthesis, and relevant, that is there is no existing equivalent review document. Another approach is evidence mapping [11], which was used by the Global Evidence Mapping Initiative in Australia [12]. Here, the number and quality of relevant studies retrieved from literature searches and their summary outcomes are tabulated for each condition or treatment of interest. A potential drawback of this approach is that it does not map the entirety of the research that could be conducted within a given clinical subject area or indeed the importance of any gaps within the evidence.

The urological cancer care pathways (UCAN care pathways from here on) being developed by our group are an attempt to address these issues. In September 2004, we facilitated plenary discussions involving urological clinicians, patients and their partners including expertise and experience of the five main cancers: kidney, bladder, prostate, testis and penis. The purpose was to better understand the needs of individuals with urological cancer in the context of

Fig. 3 Metastatic prostate cancer care pathway. For abbreviations, refer Fig. 1

their cultural setting and health system. The principal messages from patients and their families were that the following improvements are needed: (1) Better and more accessible information backed up by evidence, which could help them make decisions about their care, (2) Better care of for those that suffer unwanted effects of cancer treatment, and (3) Better support throughout their journey of care both in the clinical setting and at home. In response, a Scottish Charity (UCAN) committed funding of £2.6 million to address these gaps in urological cancer care focussed on people living in north-east Scotland but also reflecting an international perspective. Discussion with the research group on how to address the first principal message, the requirement for better and more accessible evidenced-based information for patients led to the development methodology to formulate UCAN care pathways, which we discuss in the present paper.

Our main objective is to map all plausible treatment options for each of the five urological cancers to allow collection of an appropriate range of existing and new systematic evidence reviews of effectiveness and cost-effectiveness of alternative treatment options including the magnitude of risk of short- and long-term adverse effects. We will also engage key clinical experts and patients to prioritise

unanswered questions and identify significant evidence gaps in the evidence to direct future research priorities. The ultimate aim of the UCAN care pathways is to build an evidence base for the major urological cancers and develop a framework to inform future systematic reviews, clinical practice guidelines, care algorithms, integrated care pathways and research priorities [13]. We will also work to establish a framework for wider engagement of clinicians, patients, researchers, healthcare policy makers and healthcare funders in priority setting within this clinical specialty and inform the development of a set of core outcomes for both research and clinical practices. The strength of the UCAN care pathways will be to harness and rationalise all our efforts to answering the key questions for universal benefit.

Development of urological cancer care pathways

What are care pathways?

A care pathway is a tool constructed with multidisciplinary input and used by healthcare professionals and/or researchers to map a patient's journey in terms of which treatments should be given, by whom, when, and to what outcome

Fig. 4 Hormone-resistant prostate cancer care pathway. For abbreviations, refer Fig. 1

Fig. 5 Localised renal cell cancer care pathway. Abbreviations: *HIFU* high-intensity focussed ultrasound, *CT* computed tomography, *IFA* interferon-alpha, *IL2* interleukin 2, *5FU* 5 Fluorouracil

Fig. 6 Advanced renal cell cancer care pathway. For abbreviations, refer Fig. 5

[13–16]. This broad characterisation includes many different terminologies including care profile, care protocol, critical care pathway, care map, integrated care pathway, and different uses dependent on the context, user and the stage in the research process at which it is considered. Systematic reviewers, for example, may use a care pathway to identify all plausible treatment options for a particular patient group with a view to identifying gaps in current knowledge, thereby informing possible review questions. Policy makers may use a care pathway to establish a standardised treatment algorithm for a specific clinical problem in clinical practice that can then be implemented in a particular health-care organisation [13, 17].

These examples can be seen as occupying two ends of a process: driving the research agenda on the one hand and providing a clinical useable output on the other. We see the UCAN care pathways more as being drivers of the research agenda but also providing structure for guideline developers. They are designed to inform the scope, search strategy, development and prioritisation of focussed clinical questions for relevant systematic reviews. They lend themselves well to informing development (including scope) of clinical practice guidelines rather than informing actual practice as is the purpose of clinical practice guidelines. They provide a framework for systematic review teams and guidelines panel members to identify and prioritise topic

areas, to highlight areas where guidance is currently lacking or the evidence is unclear and to reduce redundancy and resource wasting.

Methodology

Steps in the development of the UCAN care pathways

1. Definition of the aim of an individual UCAN care pathway. For example, what are the treatment options for localised prostate cancer? This will require a structured list of options and the eligibility characteristics to enter the pathway.
2. Establishment of an advisory group. This should include both clinical and methodological experts drawn from national and international professional bodies, together with representation from patient groups as lay experts and those who have experienced the disease. The purpose of the advisory group is to provide a range of user perspectives necessary to inform the development of the pathway.
3. Draughting of all plausible treatment options from the point of diagnosis moving forward to the end of treatment, follow-up and death in the form of a flow chart to producing a comprehensive but concise one-page summary.

and the clinical practice guidelines development process are relevant to all.

The aim of the search strategy for a systematic review is to maximise both the sensitivity and the specificity of the search results, that is, to retrieve all the relevant articles and exclude the irrelevant ones. In order to design the strategy, the question first needs to be translated into searchable terms using the PICO (Patient, Intervention, Comparison, Outcome) framework. The UCAN care pathways greatly facilitate this step, as all plausible interventions that can be compared are clearly shown for each patient group at every stage in the disease process. Also, the format of the pathway allows the reviewer to see where the search question is focussed in the context of the entire pathway and to see which interventions and stages of the disease are being excluded from the search. This is particularly useful when refining and reviewing the results of the search.

Prioritisation (review scope, guideline scope and development process)

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Fig. 9 Muscle invasive metastatic bladder cancer care pathway. Abbreviations: *BCG* bacillus calmette-guérin, *CIS* carcinoma in situ, *CXR* chest X-ray, *INF α* interferon-alpha, *IVU* intravenous urogram, *LUTS* lower urinary tract symptoms, *LND* lymph node dissection,

MIBC muscle invasive bladder cancer, *NMIBC* non-muscle invasive bladder cancer, *Prostatic TCC* transitional cell carcinoma of the prostate, *TB* tuberculosis

should be a process that is systematic and transparent and that includes consultation with key experts [18].

The UCAN care pathways inform the prioritisation process by providing a comprehensive framework for discussion that is applicable to multiple settings both nationally and internationally. They also inform the prioritisation process by highlighting where in the process of care the uncertainty is and the magnitude of the problem in terms of the number of people affected and its consequences. As such, they provide a concise summary of the various treatment options and inform the scope of systematic reviews and clinical practice guidelines. The UCAN care pathway model also ensures that the systematic review activity is firmly embedded in the context of the overall management of patients.

Economic evaluation and care pathways

Economic evaluation involves the comparative analysis of alternative interventions in terms of benefits such as improvement in health, the value of those improvements to

individual patients and costs [19]. An economic evaluation has to be based upon a care pathway, as an understanding is needed of what the sequence of events is from initiation of the treatment under study. The UCAN care pathways can be used to identify events that will influence a patient's well-being and events that use or save resources. Once these events have been established, they can then be measured and valued [20].

Estimates of benefits and costs can be based on data from randomised controlled trials or from a mathematical model. The models can be constructed using decision analytic methods to provide a mathematical representation of a UCAN care pathway. A model is a further level of evidence synthesis as it may incorporate the results from a number of systematic reviews.

In addition to information on cost-effectiveness, an economic model can show who stands to benefit most from use of a particular healthcare intervention and who is most likely to bear the cost. These analyses can inform judgments about equity of provision. Economic models can also be used to highlight areas for further research either by

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