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Using HTA to Identify Research Gaps: A Pilot Study

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AHFMR
ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

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The views expressed in the final report are those of the Foundation and the Institute of Health Economics.

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Authors' Note

The bulk of the pilot project was conducted in 2004. The final report was prepared in 2006.

On June 30, 2006, after 11 years at the AHFMR, the Health Technology Assessment Unit (HTA Unit) moved to the Institute of Health Economics (IHE) as part of an Alberta Health and Wellness initiative to advance the use of evidence in health care decision making by consolidating the technology assessment capacity of the HTA Unit and the economic analysis expertise of the IHE.

EXECUTIVE SUMMARY

Background and Objective

Health technology assessments (HTAs) routinely identify questions or research 'gaps' that are not adequately addressed by the primary research. The unique situation of having an HTA unit housed within a provincial research funding organization provided an ideal setting for linking research gaps pinpointed by HTAs to the funding mechanism for primary research. A pilot project was undertaken with the following objectives.

1) To assess how well HTA reports published by the AHFMR HTA unit identify research gaps.
2) To develop a process for distilling research questions from an AHFMR HTA report that could be used to inform the research funding agenda of the AHFMR. The feasibility, challenges, and implications of such an initiative will also be considered.

Methodology

An environmental scan of other HTA agencies was undertaken to identify organizations that have processes for linking research gaps identified in HTAs to the funding of health research. A literature search was also conducted to identify systematic reviews and relevant studies on the topic.

Objective 1 – To assess how well AHFMR HTA reports identify research gaps

A consecutive series four full HTA reports and four shorter reports (TechNotes) published between 2002 and 2003 by the AHFMR HTA Unit were selected for study. An independent HTA researcher who was not involved in any aspect of their production read the reports and tabulated the research gaps identified in the documents. Short face-to-face interviews were also conducted with the authors of the reports using a structured questionnaire.

Objective 2 – To develop a process for distilling relevant researchable questions from AHFMR HTA reports

Two questionnaires were developed to identify research gaps: one for researchers and one for clinicians/policy makers. The questionnaires focused on two HTA reports on chronic pain published by the HTA Unit and were piloted with a chronic pain project group comprising clinicians, government officials, and HTA researchers.

Results

From our results it appears that only two countries, Belgium and the United Kingdom, have a formal process for linking research gaps identified in HTA reports to the

research funding process. The system in the United Kingdom seems to be the most comprehensive and systematic. The literature search yielded over forty articles that discussed various issues relating to research gaps, but only one of these specifically described or assessed a method for using secondary research to identify such gaps.

Objective 1 – To assess how well AHFMR HTA reports identify research gaps

The problem of limited evidence was reported severally in the reviewed HTA reports, but research gaps were not consistently or clearly highlighted. More useful information on research gaps was gleaned from personal interviews with the researchers than from reading the reports.

Objective 2 – To develop a process for distilling relevant researchable questions from AHFMR HTA reports

All members of the project team completed the questionnaires. A summary of the questionnaire responses, reflecting the research priorities in chronic pain from three stakeholder perspectives (research, clinical, and policy), was presented to the Vice President of Programs and the Director of Grants and Awards of the AHFMR. Challenges identified included:

- balancing clinician and policy maker needs in the research design;
- incorporating consumer and public input in the process;
- assembling an unbiased group to review funding proposals;
- determining who sets research priorities;
- determining when the research question has been answered; and
- ensuring the research priorities reflect the research capacity in Alberta.

The majority of research questions identified by the pilot project are best answered by a pragmatic trial design. Therefore, HTA quality assessment criteria and synthesis methods must be expanded to encompass pragmatic trials.

Conclusions

A process was developed for distilling research gaps identified in HTAs on chronic pain management into researchable questions that a provincial research funding body, in this case the AHFMR, can use to inform its research agenda. This novel approach also identified a research team to coordinate and potentially conduct the necessary research studies. The HTA Unit can make this process more efficient by identifying and explicitly describing research gaps in its reports and involving clinicians, policy makers, consumers, and the public in the production of HTAs.

Establishing a process that uses HTA results to identify gaps in research will likely encourage more balanced funding of pragmatic and explanatory trials and promote the use of HTA and research evidence by decision makers in the health system.

TABLE OF CONTENTS

Tables and Figures:

SCOPE OF THE REPORT

Health technology assessments (HTAs) routinely identify questions or research 'gaps' that are not adequately addressed by the primary research. In Alberta, the unique situation of having an HTA unit housed within a provincial research funding organization, the Alberta Heritage Foundation for Medical Research (AHFMR), allowed an exploration of the feasibility of linking future research needs pinpointed by HTAs to the funding mechanism for primary research. This report describes a pilot project initiated by the AHFMR HTA Unit to achieve the following objectives.

1) To assess how well HTA reports published by the AHFMR HTA unit identify research gaps.
2) To develop a process for distilling research questions from an AHFMR HTA report that could be used to inform the research funding agenda of the AHFMR. The feasibility, challenges, and implications of such an initiative will also be considered.

INTRODUCTION

What is health technology assessment?

In most countries, the demand for health care far outstrips the resources available to provide it. This imbalance has led to the development of health reforms that ensure universal access and equity, and simultaneously improve the efficiency and quality of health care by controlling costs and promoting the use of cost effective treatments. As a result, opinion based decision making, at least as an overt method of choosing health policy, is in decline. Decision makers within the healthcare system are now expected to make explicit, public decisions that are based on scientific evidence, even if the final decision is still predominantly influenced by other factors such as personal values and resource considerations.[1]

These imperatives have contributed to the rise of health technology assessment (HTA), a form of policy research that systematically examines the effects of a particular technology on the individual and society with respect to its safety, efficacy, effectiveness and cost-effectiveness, and its social, economic, and ethical implications, and identifies areas requiring further research in order to inform decision making in both policy and practice.[2,3] In this instance, a health technology can be defined as any intervention that is administered with the aim of improving the health status of patients or of populations.[1] This includes drugs, devices, procedures, and the organizational and support systems within which health care is delivered.[3]

By definition, HTA does not generate knowledge for its own sake but rather assesses topics that are of current importance to society. HTA improves 'value for money' in health care by ensuring that the medical technologies introduced are safe, efficacious, and appropriately used.[3] HTA activities are currently undertaken in more than 21 countries, and the majority are publicly funded and administered by national or regional governments.[4]

HTA and knowledge gaps

The activity of HTA has often been characterized as a bridge or link among researchers, policy makers, and clinicians that can facilitate the direct translation of scientific and medical research into improvements in clinical practice and patient care. Nonetheless, HTA agencies have often been accused of working in a relevance vacuum and producing reports that have little or no obvious effect on clinical practice or health policy. Consequently, many HTA agencies have initiated impact analysis projects to assess how HTA reports are used by decision makers in the healthcare system, and how this utilization can be improved in the future.[5] The latter goal has spurred the development of knowledge brokering activities in both the clinical and policy making domain.

Thus, the knowledge gaps that exist in clinical practice with respect to what works and what doesn't have been heavily scrutinized and are the focus of many initiatives designed to transfer scientific research results into clinical practice. However, the traffic on this HTA 'bridge' connecting researchers, policy makers, and clinicians is currently only one way. There is another important HTA 'bridge' linking these groups which has elicited far less attention.

The relevance gap in health research

In most countries, basic research is mainly supported by public funds, while the private sector often concentrates on applied research and technology development. In health this means that industry primarily concentrates on the development of drugs and medical devices, whereas medical and surgical procedures are usually developed in large academic medical centres. A major problem with this arrangement is that developments from industry are often driven by technological and monetary factors rather than the health needs of the population.[3]

In addition, publicly funded academic institutes commonly produce research that does not address a relevant patient need or improve on previous inconclusive studies, and may even duplicate prior work on a question that has already been adequately answered. An excellent, albeit frightening, example of this was the continued use of placebos in trials assessing the use of antibiotic prophylaxis for colorectal surgery when convincing evidence from more than a dozen trials had already shown that antibiotics reduced postoperative mortality. This represents both an inefficient use of limited research resources and an ethical issue for the study participants who were denied an obviously beneficial treatment.[6]

Despite substantial increases in public and private funding for clinical research over the last decade, research output still fails to provide answers for many common, important clinical questions.[7,8] This is most apparent in the conclusions of systematic literature reviews, HTA reports, and clinical practice guidelines. These research syntheses are designed to provide a comprehensive summation of the available evidence for decision makers in the healthcare system, but this aim is routinely stymied by the poor quality and inadequate quantity of the available evidence.[9] In addition, research on new treatments often asks the wrong questions, which severely limits its public health relevance.[7,8,10]

This relevance disconnect between the research agenda and societal need has significant consequences. It undermines efforts to improve the scientific basis of healthcare decision making and limits the ability of public and private insurers to develop evidence based coverage policies. This often results in millions of dollars being spent on treatments that have no demonstrated benefit, often at the expense of treatments whose benefits have yet to be shown. In the meantime, basic research continues to

generate more and more health technologies that will be added to the list of poorly evaluated, usually expensive, and potentially ineffective and/or lethal treatments.[9]

Identifying the research gaps

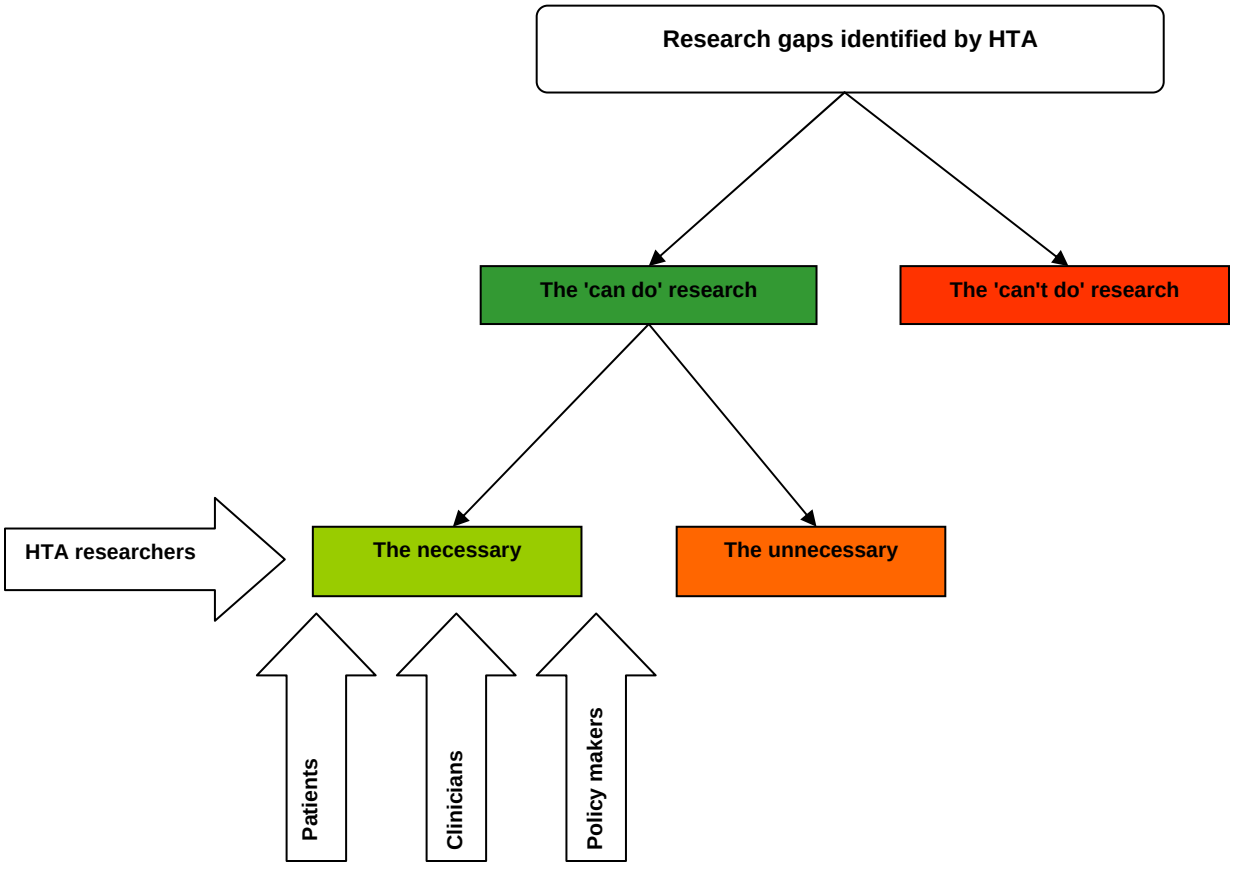
Clinical trials designed to provide answers to questions asked by healthcare decision makers are referred to as pragmatic or practical clinical trials. They assess effectiveness, the extent to which an intervention produces a result under ordinary circumstances.[11] In contrast to explanatory or mechanistic trials, which recruit homogeneous populations and determine how an intervention works under ideal conditions (efficacy), pragmatic clinical trials are formulated according to the information needed to make a decision and are conducted in heterogeneous patient populations under 'real world' conditions.[9,10,12] Pragmatic trials are concerned with which treatment or therapy works, not how it works.[7] Neither methodology is superior, nor can a single study design adequately capture all the information needed to assess the usefulness of an intervention.[13] Ideally, both trial types should be represented in the research funding agenda.

It is generally recognized that research is crucial to controlling the growth of healthcare costs because it can help identify innovative, lower cost alternative therapies that should be promoted, as well as costly, harmful, and ineffective treatments that should be sidelined.[14] The majority of trials conducted to date have been explanatory trials, which some claim are so far removed from clinical practice in the real world that they are of little practical value.[7] This imbalance has occurred because most major research funding organizations do not have an explicit mandate to fund clinical studies that are important to decision makers. In an attempt to redress this, the National Institutes of Health in the United States have funded a number of pragmatic trials that have provided valuable information for clinical and health policy decision makers.[9] In addition, most of the US$60 million that is allocated for clinical trials by the Department of Veterans Affairs in the United States has been used to conduct pragmatic clinical trials. Research funding bodies in Canada have also sponsored a number of pragmatic trials in recent years.[9,13]

However, these funding organizations do not have a systematic mechanism for identifying the priority areas of decision makers.[9] HTA reports are an as yet unexploited source of systematically generated, comprehensive information on the gaps in medical research. They routinely identify questions or 'research gaps', which are not adequately addressed by the available primary research, as potential areas for future research. In the past, HTA agencies have been criticized for producing inconclusive reports that make vague calls for 'more research'. To counter this, many agencies now make explicit recommendations about the kind of research that is needed to fill the identified research gaps.

In an ideal world all of these gaps would be filled. However, the reality is that ethical considerations, limited funding and expertise, and small patient populations, to name a few, can stall clinical research and result in questions that are never satisfactorily answered; i.e. the 'can't do' research (Figure 1). Therefore, the areas of future research identified in HTA reports must be prioritized. The 'necessary' research is the minimum amount of additional information required for decision makers to be able to make a decision that they can live with. Exactly what this information is will depend upon whom you ask. For example, clinicians may be interested in quality of life issues, while policy makers may be more focused on the economic implications of implementing a new intervention. Relying solely on the producers of HTA reports to identify research gaps will result in an objective and exhaustive list, but not necessarily one that is relevant to medical practice.[15] Thus, it is essential that any endeavour to identify research gaps includes researchers, policy makers, clinicians, consumers, and the public, since each group will often have different opinions on how future research should be designed, financed, and developed.[16,17]

Figure 1: Diagram of the conceptual framework for determining research gaps



Using secondary research to inform the research funding agenda

Using HTA to increase the relevance of research to health policy is in its infancy. However, there is an increasing trend in many countries to set priorities for research, especially in applied or clinical areas, that are based on secondary research. The principle of using systematic reviews of relevant evidence to inform decisions on whether to fund new research or continue the support of ongoing research is spreading.

In 1997, the Danish National Research Ethics Committee System concluded that research groups should conduct a review of all the relevant literature prior to submitting a research proposal. The National Health Service (NHS) governance arrangements for the NHS Research Ethics Committees in the United Kingdom state that research which duplicates prior work, or is so poorly designed that it is not likely to extend existing knowledge, is unethical.[18] In fact, the NHS HTA program and the Medical Research Council have put in place mechanisms to ensure that information from systematic reviews of past research is available to guide decisions about research funding. The NHS program systematically scans various research resources to identify recommendations for research based on identified knowledge gaps. The Medical Research Council now requires funding applicants to supply references for systematic reviews and discuss the need for their proposed research in light of the review evidence. If systematic reviews do not exist, details of the search strategy used to identify existing trials must be provided. This not only avoids duplication of effort and wasted funding, but also promotes collaboration and appropriate replication of research work.

The Essential National Health Research program in the Philippines also has a research agenda that is derived from a review of existing literature to identify research gaps, together with direct consultation with policy makers, program managers, and the public, to ensure that the research agenda answers an identified and prioritized need.[19]

The health research funding milieu in Alberta

The Alberta Heritage Foundation for Medical Research (AHFMR) was established by the Government of Alberta in 1980 to fund biomedical and health research in the province of Alberta, Canada. A portion of the interest revenue generated from the initial government endowment of CN$300 million has been used to provide more than CN$700 million in research funding to the scientific community over the last two decades. The AHFMR awards over $40 million in grants and awards each year and is one of the main sources of public funding for medical research in Alberta.[20]

The primary goal of the AHFMR is to improve the health and quality of life of people in Alberta and worldwide through the generation and application of health research knowledge. The research grants are disbursed via a system of peer review, whereby applications for funding are assessed for their feasibility, importance, and originality by external reviewers with expertise in the relevant field. The applications are then ranked

by an AHFMR committee of reviewers.[20] While the AHFMR designates broad research areas for different categories of funding, there is no mechanism for systematically and objectively identifying existing gaps in the research. Therefore, the HTA Unit of the AHFMR undertook a pilot project to develop a process for linking the future research needs or 'research gaps' pinpointed by HTA Unit reports to the funding mechanism for primary research in Alberta.

METHODS

In Alberta, a unique situation exists in which an independent, government sponsored HTA unit is housed within a provincial research funding organization, the AHFMR. This provided an ideal setting for the pilot project.

Literature search

A systematic search of the medical literature was conducted to identify systematic reviews and relevant studies of any design on similar projects undertaken by other organizations. Searches were conducted without language or date restriction (Appendix A). The bibliographies of all publications retrieved in full hard copy form were manually searched for relevant references that may have been missed in the database searches.

Additional searches were also run in April 2006 on Google.com and Copernic.com to locate grey literature using the key terms: research gap, knowledge gap, practical trial, and pragmatic trial.

Environmental scan of other HTA agencies

The International Network of Agencies for Health Technology Assessment (INAHTA) comprises 43 member agencies in 21 countries from North and Latin America to Europe, Australia, and New Zealand.[4] Through INAHTA's web page, the websites of all the member agencies were accessed to identify organizations that have processes for linking research gaps identified in HTAs to the funding of health research.

An email questionnaire was also sent to the INAHTA agencies asking representatives specific questions about activities in this area with respect to:

- who is involved in the process;
- how are the research gaps identified and translated into researchable questions; and
- how are the researchable questions fed into the funding mechanism for health research?

We also asked for links to or electronic copies of documents that describe the process.

Identifying research questions from HTA reports

Objective 1 – To assess how well AHFMR HTA reports identify research gaps

The Assistant Director of the HTA Unit selected a consecutive sample of four of the most recently published full HTA reports and four shorter reports (TechNotes) (Table 1). An independent HTA researcher who was not involved in any aspect of their

production read the reports and tabulated the research gaps and opportunities identified in the documents.

Table 1: List of the sampled HTA reports and TechNotes

Report Type	Title/Publication Date
Health Technology Assessment	Prevalence of chronic pain: an overview (HTA 29) (2002)[21]
Health Technology Assessment	Multidisciplinary pain programs for chronic pain: evidence from systematic reviews (HTA 30) (2003)[22]
Health Technology Assessment	Islet cell transplantation for the treatment of non-uremic type 1 diabetic patients with severe hypoglycaemia (HTA 31) (2003)[23]
Health Technology Assessment	Surgical treatments for deep venous incompetence (HTA 32) (2003)[24]
TechNote	Osteogenic protein-1 for fracture healing (TN 37) (2002)[25]
TechNote	Treatment of thoracic insufficiency syndrome with the vertical expandable prosthetic titanium rib (TN 38) (2002)[26]
TechNote	Trigger point injections for non-malignant chronic pain (TN 39) (2002)[27]
TechNote	Sclerotherapy for varicose veins of the legs (TN 40) (2003)[28]

Short face-to-face interviews 1 hour or less) were conducted with the authors of the reports using a structured questionnaire (Appendix B) that asked for information on: the process of writing the report; the quality of the studies included in the analysis; the research, clinical, and political issues identified; and the existence of ongoing clinical trials. The questionnaire was also given to the Vice President of Programs and the Director of Grants and Awards of the AHFMR prior to its use to derive feedback on its design.

Objective 2 – To develop a process for distilling relevant researchable questions from AHFMR HTA reports

Two HTA reports on chronic pain were selected; one on prevalence and the other on the use of multidisciplinary treatment programs.[21,22] These reports were chosen for two reasons. Firstly, the issue of chronic pain is topical and becoming increasingly important in Alberta. Secondly, a unique interdisciplinary Information Sharing Group on Chronic Pain, comprising clinicians, health ministry officials, and HTA researchers, had formed in an ad hoc fashion during the development of these two HTAs to provide advice and comments on the draft reports. The Group continues to meet on a regular basis, in association with the AHFMR HTA Unit, and is currently involved in a number of chronic pain research initiatives in Alberta. Thus, the members were easily accessible

for interviewing, highly motivated to contribute to the pilot initiative, and covered a broad cross-section of stakeholder interests.

Two questionnaires were developed, one for HTA researchers and one for clinicians/policy makers (Appendix C), and sent to the participants 2 weeks prior to the scheduled interview. All interviews were conducted either face-to-face or via telephone. The interviews were transcribed directly into a computer and then summarized. Each respondent was sent a copy of his/her summarized responses to provide feedback and make corrections.

RESULTS

Literature Search

The literature search yielded over forty articles that discussed various issues relating to research gaps, but only one[15] described or assessed a method for using secondary research to identify such gaps.

The Dutch Organisation for Scientific Research attempted to identify the gaps in research on the effectiveness of therapeutic interventions for nine non-malignant chronic pain syndromes.[15] A survey was conducted among all the relevant medical and related disciplines to identify which therapeutic interventions were commonly used in the Netherlands. A systematic review of the literature on these interventions was then carried out. This generated a list of interventions with proven effectiveness or lack of effectiveness, and another list of interventions for which either new systematic reviews or primary studies were needed. The members of four centres of expertise in the treatment of chronic pain participated in a consultative process, using a combined Delphi method and nominal group technique, to generate a prioritized list of research gaps from the interventions identified as having an inadequate evidence base. Although the final list was not actually used to program research funding, the authors concluded that the method was both practical and useful for identifying knowledge gaps in applied medical research when the topic area is clearly demarcated. However, the method was not considered useful when the objective is to search for new, innovative treatments.[15]

Environmental Scan

Twelve INAHTA agencies from eleven countries responded to our questionnaire (Table 2). From our results it appears that only two countries, Belgium and the United Kingdom, have a formal process for linking research gaps identified in HTA reports to the research funding process. The system in the United Kingdom is facilitated by two agencies, NCCHTA and NICE, and seems to be the most comprehensive and systematic. The NCCHTA has a specific budget for this activity. The linkage of research gaps to future research funding among the other nine agencies is not formalized and usually occurs in an ad hoc, serendipitous fashion, if at all. Many HTA agencies are keen to learn more from foreign experiences and results in this area before attempting to establish a process of their own.

Table 2: Summary of the INAHTA member survey results and environmental scan

Agency/Country	Information Source	Formal Process	Details
Institute of Technology Assessment (ITA) Austria	Personal communication	No	
Belgian Health Care Knowledge Centre (KCE) Belgium	Personal communication	Yes	If unanswered questions are identified by HTA reports, a new topic proposal on these questions can be submitted for the work program of the following year. Topic proposals are reviewed yearly and a selection is made based on their relevance to health policy or potential impact. The selected topics are examined as part of the work program of the KCE. Retained topic proposals are funded by the KCE. Either the research is done in-house or outsourced to external interested parties, depending on the available expertise at the KCE or elsewhere in Belgium.
Agence d'evaluation des technologies et des modes d'intervention en santé (AETMIS) Canada	Personal communication	No	
Danish Centre for Evaluation and HTA (DACEHTA) Denmark	Agency website Personal communication	No	No formal activity, but in certain cases the agency financed PhD programs in specific fields that needed more research.
Hungarian HTA agency (HunHTA) Hungary	Personal communication	No	
The Advisory Council on Health Research (RGO) Organization for Health Research and Development (ZonMw) Netherlands	Personal communication	Unclear if topics for future research come from HTA reports	A subprogram of the Health Care Efficiency Research Program (annual budget of EU€12.2 million) focuses on closing the remaining knowledge gaps to promote the use of cost-effective interventions. Details of the process are unclear. The RGO sets priorities for the HTA program of ZonMw, which then invites researchers to formulate research proposals on the specific research topics.

Table 2: Summary of the INAHTA member survey results and environmental scan (cont'd)

Agency/Country	Information Source	Formal Process	Details
Norwegian Knowledge Centre for the Health Services (NOKC) Norway	Personal communication	No	A discussion has been started to get something in place. Collaboration with the Norwegian Research Council and other main research financing institutions (big hospitals) is important.
The Catalan Agency for Health Technology Assessment and Research (CAHTA) Spain	Agency website	Unclear if topics for future research come from HTA reports	The agency designs and assesses research protocols and projects. CAHTA manages a biennial call for clinical and healthcare services research proposals that are financed by the CatSalut and the Inter-department Research and Technological Innovation Commission (CIRIT).
Basque Office for Health Technology Assessment (OSTEBA) Spain	Personal communication	No	
The Swedish Council on Technology Assessment in Health Care (SBU) Sweden	Personal communication	No	There are future plans to inform the Deans of Medicine of the Universities of the knowledge gaps identified by HTAs. The SBU also plans to offer some compensation for the time spent by researchers in writing research grant applications.
The Health Technology Assessment Program (NCCHTA) United Kingdom	Agency website Personal communication	Yes	There is a formal section in HTA reports identifying further research required. This is fed into the NCCHTA prioritization process, together with research recommendations from other high quality systematic reviews of research evidence, Cochrane Reviews, guidance issued by the National Institute for Health and Clinical Excellence, and other NHS Programs. The HTA program invites bids to do the prioritized research with an annual budget of GB£10 million. The Health Technology Assessment Commissioning Board (HTACB) oversees the commissioning process.

Table 2: Summary of the INAHTA member survey results and environmental scan (cont'd)

Agency/Country	Information Source	Formal Process	Details
National Institute for Health and Clinical Excellence (NICE) United Kingdom	Agency website	Yes	See NCCHTA. One objective of the Research and Development Programme, which was established in 2003, is to fill evidence gaps identified in NICE reports. Research recommendations are actively promoted to research funding bodies. Research funded by the program is normally commissioned in partnership with another organization rather than directly funded by the program itself.
The Agency for Healthcare Research and Quality (AHRQ) United States	Personal communication	No	The AHRQ Evidence Reports usually have a section regarding research gaps, but there is no formal process for feeding this into health research funding. Funding of research for identified knowledge gaps is considered the responsibility of the proponents of the technology or the HTA requestors. Occasionally requestors of the initial HTA will stimulate other agencies to conduct the needed research identified by the HTA. The process seems to work better when the funding organization requests the report.
Veteran Affair's Technology Assessment Program (VATAP) United States	Personal communication	No	Some VATAP HTAs have resulted in follow up research studies, but whether reports are linked to funded research or not depends on the requestor of the HTA and their initial intent.

HTA – health technology assessment; NHS – National Health Service

Identifying research questions from HTA reports

Objective 1 – To assess how well AHFMR HTA reports identify research gaps

The problem of limited evidence was reported severally in the selected reports[21-28] with reference to the paucity of good quality studies available, short follow-up periods, absence of economic evaluations, and lack of information concerning the efficacy, effectiveness, and safety of the health intervention analyzed. However, these research gaps were not consistently or clearly highlighted in the reviewed HTA reports. In addition, the following problems were identified.

- More useful information was gleaned from personal interviews with the researchers than from reading the reports.

- The research priorities identified by a HTA researcher in isolation do not necessarily reflect those of policy makers or clinicians.
- Feedback from the Vice President of Programs and the Director of Grants and Awards at the AHFMR emphasized the need for results that move beyond the relatively vague statements about "more research being needed" and "better studies required" that were routinely found in the HTA reports.

Objective 2 – To develop a process for distilling relevant researchable questions from AHFMR HTA reports

All six members of the Information Sharing Group (one policy maker, one policy maker/health services researcher, one clinician, one clinician/health administrator, and two HTA researchers) agreed to participate. One of the HTA researchers from the Information Sharing Group was also involved in designing the questionnaires. Therefore, to avoid any bias, this individual was not surveyed. The remaining five participants completed the questionnaires on the two HTA reports (Tables 3 and 4). As some of the participants had multifaceted roles, they were designated by their primary area(s) of responsibility as follows: Policy A, Policy/Health Services (HS) Researcher B, Clinician A, Clinician/Administrator B, and HTA Researcher. The questionnaire results (Appendix D) were compiled into a list of research priorities in chronic pain that reflected the three stakeholder perspectives (health services research, clinical, and policy).

Research gaps identified from an HTA report on the prevalence of chronic pain

Table 3: Summary of the HTA report

Report	Scope	Research gaps/opportunities noted in the text of the report per Objective 1
Prevalence of chronic pain: an overview (HTA 29) (2002)[21]	Objectives were to: 1. To present and critically appraise the published evidence on the prevalence of chronic non-malignant pain in the general population and primary care setting in Alberta. 2. To summarize evidence from primary studies on the characteristics of pain and the use of health services by chronic pain sufferers.	To conduct concurrent, prospective epidemiological studies to estimate the chronic pain prevalence in Alberta. To improve the methodological approaches for studying the prevalence of chronic pain.

Research gaps identified per Objective 2

What are the main research and clinical questions that remain unresolved after reading this report?

a) To establish a standardized definition of chronic pain that is agreed upon by the entire pain community and defines severity in terms of quality of life and heath service utilization.

b) To establish a scale that quantifies the gradations of severity within the experience of chronic pain.

c) (i) What is the prevalence and incidence of chronic pain:

- in Alberta;
- that is associated with various underlying pathologies, such as diabetes or migraine;
- in certain population groups, such as the elderly, or males or females?

(ii) What research variables, such as outcomes and data collection methods, affect the prevalence estimates?

(iii) If either prevalence or incidence is unstable, what risk factors, such as environmental factors, are responsible?

d) Does the utilization of health services change for different diseases once chronic pain is alleviated?

What are the main policy questions that remain unresolved after reading this report?

a) What is the threshold at which the health system should provide health services?

b) What health resources should be allocated and to whom?

What kind of information/data/study would best answer the unresolved issues?

- Prevalence could be determined using prospective primary studies in combination with epidemiological studies of administrative data from the Health Ministry.
- Retrospective studies using chart review and linking patient data to utilization data would also be valuable.
- The research group should include an epidemiologist, a health economist, and clinical advisors.

Research gaps identified from an HTA report on multidisciplinary pain programs

Table 4: Summary of the HTA report

Report	Scope	Research gaps/opportunities noted in the text of the report per Objective 1
Multidisciplinary pain programs for chronic pain: evidence from systematic reviews (HTA 30) (2003)[22]	Prepared in response to a request from Calgary Health Region and Alberta Health and Wellness for updated evidence on the efficacy, effectiveness, and economic outcomes of multidisciplinary pain programs for chronic non-malignant pain.	Need for a standardized operational definition of multidisciplinary pain program to enable meaningful program comparisons or evaluations. Need for research on the various aspects of the multidisciplinary pain program approach to determine which treatment or set of treatments is responsible for the observed improvements and which kind of patients do best under a particular form of individualized treatment plan. Need to monitor outcome data and measure quality of life.

Research gaps identified per Objective 2

What are the main research and clinical questions that remain unresolved after reading this report?

a) A standardized definition of multidisciplinary pain programs needs to be established.

b) A universal, comprehensive set of standardized outcome measures, which include psychological, economic, quality of life, functional, pain severity, and service utilization measures, needs to be compiled to enable inter-program and inter-study comparisons.

c) What is the efficacy or efficiency of individual multidisciplinary program components?

d) What is the effectiveness of multidisciplinary pain programs for indications other than low back pain and pelvic pain?

e) What level of service should patients receive according to their pain severity?

f) Cost effectiveness must be established with respect to:

- various pain conditions;
- single interventions, such as chiropractic care;
- community care (family doctor in combination with specialty consults).

What are the main policy questions that remain unresolved after reading this report?

a) What is the cost utility of multidisciplinary pain programs?

b) Who needs multidisciplinary pain programs, and what types of multidisciplinary pain programs work for which patient groups?

c) Is the treatment effect of multidisciplinary pain programs durable?

d) A tool is needed to triage patients into different pain programs according to their needs.

What kind of information/data/study would best answer the unresolved issues?

- A more rigorous systematic review with broader inclusion criteria is needed to address some of the questions identified.
- A field evaluation of the current multidisciplinary pain programs in Alberta is needed.
- A comparative controlled study conducted over a minimum of five years, with follow up at six months, one year, and then annually, could be used to compare multidisciplinary pain programs with community care.
- The research group should include health economists, clinical researchers with program skills, psychologists, and community health researchers.

Engaging the funding agency

The above summary of questionnaire responses, reflecting the research priorities in chronic pain from three stakeholder perspectives (research, clinical, and policy), was presented to the Vice President of Programs and the Director of Grants and Awards of the AHFMR. A meeting was convened to obtain feedback on how their needs were met, what they thought of the process, and their interest in providing dedicated funds for the research proposals generated.

The consensus was that the process held promise. The main points derived from the meeting were as follows:

- A dedicated group needs to be identified that will have the commitment to shepherd the process from start to finish.
- Researchers drive the research funding agenda in Alberta, so a paradigm shift is required. The research gaps project may be an important step in achieving this.
- The level of simplicity of the process should reflect the dollars available.
- It is important for HTA to link the stakeholders.
- This process may work on a case by case basis.
- The AHFMR does not currently have an identified mechanism for pinpointing research needs. Using HTAs to identify research gaps may be a way to do this.

- Currently at the AHFMR the majority of research funding is allocated via a protected, planned, and closed process. A more open process would be required to allocate funding for research gaps identified in HTA reports.
- Any process needs to take into account the research capacity in Alberta, and whether the results will actually benefit Albertans.
- The questionnaire results need to be distilled further into more specific researchable questions.

DISCUSSION

Recent discussions on the development of a comprehensive Canadian strategy for HTA, which involved 36 participants from the policy community, health regions, providers, and organizations involved in HTA within Alberta, identified several key messages.[29] One of these was the need to address the gaps in the research evidence that limit HTA analysis, and to identify mechanisms through which HTA can influence the primary research agenda of national and provincial funding bodies. The research gaps pilot project was a first attempt at meeting this need by developing a workable process to link research gaps identified in HTA reports to the funding mechanism for health research at the provincial level. While this was in essence a feasibility project, it also became an avenue to engage the AHFMR in an ongoing initiative that would have a life beyond that of academic curiosity.

It is clear that HTAs must be more explicit in defining specific research questions in order to be a facilitating factor in setting the research agenda. However, this cannot be done in a contextual vacuum. The pilot project demonstrated the importance of incorporating input from motivated stakeholders from the clinical and policy arenas. It also provided a method of formulating the most important researchable questions and identifying a potential research team to conduct the necessary studies.

One major limitation of this project was that input from the public was not sought. This must be rectified in future iterations of the process to ensure that all stakeholder views are adequately addressed when identifying and prioritizing the researchable questions. Another limitation is that no criteria were used to select the HTA reports used in the pilot project. Since it is unrealistic to expect that all HTA reports produced by the AHFMR HTA Unit will undergo this process, formalized, objective criteria for prioritizing which HTA reports are chosen must be developed. In addition, the project has only gone as far as developing a method that could be used to identify researchable questions (Figure 2). The next step is to actually formalize the prioritization and funding process. A number of questions and challenges present themselves as we move forward.

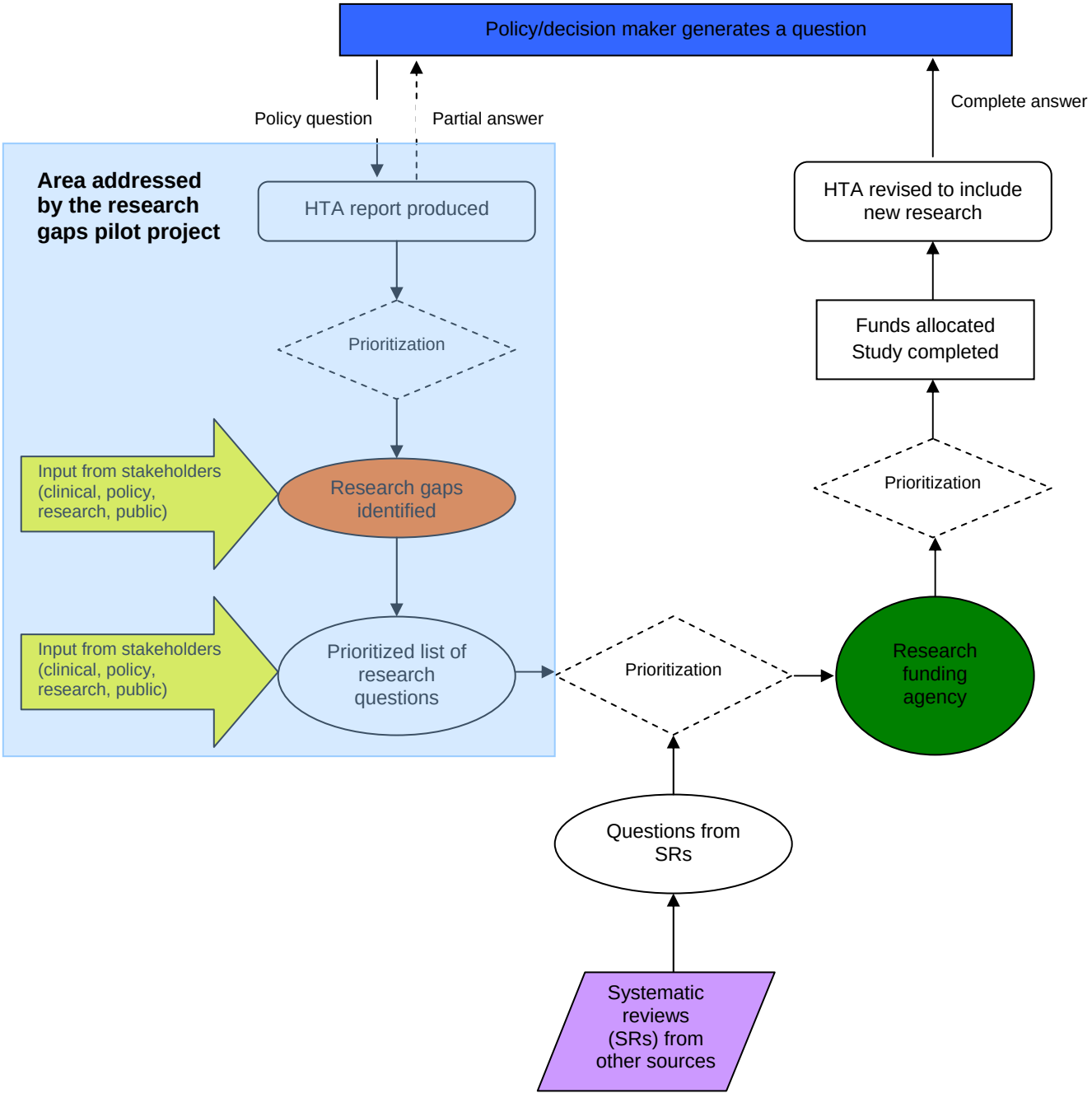
Further considerations and challenges

Implementation issues

Prioritizing the research questions

It is often said that research is a cumulative effort that is rarely definitive. From this point of view, if past research does not inform the planning of future studies it becomes pointless. Most endeavours in the business and policy realm spend at least a small

Figure 2: Flow diagram of the conceptual framework for the feedback loop involving research gaps identified by HTAs



portion of their budget on determining whether the money has been spent well, but this is rarely done in health research.[30] It has been suggested that research funding decisions should be based on an assessment of the expected net value of the research and whether the projected improvements in knowledge justify the cost.[30] While this may seem overly exacting and mercenary, in cases where the research is aimed at refining the existing knowledge base this may be a way of ensuring that research is innovative rather than duplicative. Decision analysis and value of information analysis are increasingly being applied to research prioritization in order to ensure the greatest gain from the funds available.[31]

Priority must be given to research that is most likely to improve health.[32] The NHS R&D program in the United Kingdom owes its genesis in 1991 in part to a concern that the predominantly science-led research agenda of the previous decades was creating an evidence vacuum and depriving clinicians and health service managers of data on the effectiveness of care that they needed to make informed decisions. Ironically, although the NHS was the "principal customer" for research output, it had little input into the initiation of research programs. Even now, though the R&D program funds both clinical and health services research, the majority of funds still go to scientific research. In addition, the program is still grappling with how to prioritize the research agenda and involve consumers and the public in its processes.[33]

Any prioritizing process must be complex enough to be rigorous, unbiased, and inclusive, but not be so daunting, laborious, or overly bureaucratic as to deter would-be researchers. In cases where a number of researchable questions are identified from an HTA with no clear front runner, there must be an established process outlining who is responsible for prioritizing these questions and the criteria used. The responsibility for developing such a process will most likely lie with the funding body. Careful consideration must be given to how much time and money is spent on such a process, and assembling an unbiased, representative group to review the funding proposals may be challenging. In addition, the entire process must be shepherded to ensure that it is timely, the research gap proposals do not get sidelined by other funding priorities, and the needs of all stakeholders are taken into account in the research design. Another consideration is the perceived ownership of the research dollars currently in the system. Additional targeted funds may need to be found for identified research gaps, rather than shifting money within the pool of currently available dollars, to ensure acceptance by stakeholders in the research community.

The prioritization process must also be informed by the mandate of the funding agency and the research capacity within their jurisdiction. This is particularly relevant for Alberta, which has a sizable pot of research money available (just over $45 million disbursed in the 2004/2005 financial year) but only three million residents.[34,35] The AHFMR is specifically established to meet the needs of Albertans, so questions identified in HTA reports, which are often based on international research, must

balance international needs with those of Alberta and be contextualized against local needs. In addition, the research capacity within the province needs to be considered. If Alberta does not have the required clinical expertise for a given research proposal, consideration needs to be given as to whether an out-of-province collaboration should be pursued, and where the additional research dollars will come from. In Canada, potential funding partners include the Canadian Institutes of Health Research, the Canadian Health Services Research Foundation, and the Canada Foundation for Innovation. The role of other HTA agencies in Canada, such as the Canadian Agency for Devices and Technologies in Health (CADTH), in coordinating and establishing research policy also needs to be ascertained to ensure a unified strategy. For example, the Ontario Health Technology Advisory Committee has already established a Program for Assessment of Technology in Health (PATH) that undertakes field evaluations to collect primary data in parallel with an HTA for new technologies that have a scant evidence base.[36]

In countries where a number of different organizations distribute research funding, differing priorities can lead to deficiencies in research capacity. For example, the United Kingdom is sometimes beset by a lack of researchers in priority areas because of a priority disconnect between tertiary educational institutions, which traditionally give more weight to basic than applied research, and NHS R&D program priorities.[33] This situation is unlikely in Alberta, where the majority of research funding comes from the AHFMR, but ensuring alignment between the goals of universities and research funding bodies is nonetheless an important piece of the puzzle.

Using HTA to identify research gaps may aid in expanding the research agenda to include more traditionally underserved research areas, such as treatments for uncommon diseases. Such conditions are often the subject of HTAs because they usually have a significant effect on health and can be costly to treat. Conversely, such a process could also be used to identify research that should not be done. However, care must be taken to ensure that explanatory trials and basic curiosity driven research are not under funded as a result of an increased focus on policy related research.[37,38] A more equitable split of research dollars should be the primary aim of this endeavour. Indeed, increased efficiency in the use of research dollars would allow greater support of explanatory trials.[38]

Role of the HTA researcher(s)

The underlying assumption of this project was that once the researchable questions were identified they would be presented to the funding agency, which then had the responsibility of seeing that they were adequately acted upon. Indeed, the HTA researcher was not asked about the design, formulation, or execution of future studies in the questionnaires (Appendix C, Question 4). However, the role of the HTA researcher in the subsequent funding process should be more clearly defined, particularly with respect to the planning and design of future research.

Obtaining clinical, policy, consumer, and public input

Our results highlighted the fact that the research questions identified varied with the respondent's background (Appendix D), thus emphasizing the need for multiple perspectives to increase the relevance. In addition, shades of difference were seen between individuals within the clinician and policy groupings, depending on their interests, roles, and educational background. It was also evident that the funding environment can influence how people answer the questionnaire, particularly clinicians who may be future applicants for the research funds resulting from the research gaps identification process.

This pilot project was successful in no small part due to the serendipitous existence of the Information Sharing Group, which provided a pool of accessible, motivated, and knowledgeable clinicians and policy makers who could participate in the process. However, in most cases such a group is not likely to be available, so who then provides clinical and policy input? And who provides public input? A permanent board or panel is not appropriate because the expertise of the membership would have to be different for each intervention. One possible solution is to engage the policy maker(s) who asked the question in the first place and the clinicians who were either external reviewers for the HTA report, or who may have provided clinical expertise during its synthesis. Professional organizations may also be able to identify clinical experts, and lobby groups and consumer advocacy agencies may be a potential source of consumer participants. Involving the public and consumers in the production of HTA reports, rather than just at the tail end, would make this process even more seamless.

The NHS R&D program in the United Kingdom has already attempted to include consumers in a process to identify research priorities, with some success.[39] Like our pilot project, they found that face-to-face discussion with the participants was the most fruitful way of obtaining the required information. In Alberta, it is also important to ensure that a representative sample of people from both the urban and non-urban health regions is consulted.

Incorporating policy, consumer, and public input into the prioritization process would have major implications for the way the AHFMR funds research because none of these groups are included in the peer review process used to assess research proposals at present.

Feedback loop

For the research gaps identification process to be effective, the funded research needs to be fed back into another HTA, or some other mechanism, to provide the answer to the decision maker who originally asked the question and close the loop (Figure 2). This means that criteria may need to be established at the outset for determining when the question has been answered. These criteria may also be a useful way of gauging whether the research dollars were well spent. This cycle may have to go though a

number of iterations before there is sufficient evidence upon which to base healthcare decisions.[40] Consequently, good coordination and communication between all the actors in the process is essential for success, and the process must be timely to ensure that the end result is still relevant to the policy maker and the current clinical context.

One respondent in our project (Clinician A) noted that more clinicians would be willing to invest their time in providing input to HTAs if funding was provided for studies that are generated by research gaps identified in the reports. While this may potentially bias the research gaps identification process, it will probably strengthen the feedback loop. In addition, practitioners may be more willing to participate in trials that answer questions they helped to generate and are relevant to clinical practice.

Methodological issues – pragmatic versus explanatory trials

> *"…clinical practice not based on evidence is unplanned experimentation, from which learning is unlikely to occur…".*[41]

Some people consider research as an activity that is distinct from the practice of medicine. However, this view is slowly being usurped by the alternative perspective that clinical research is inextricably linked to clinical practice. To create knowledge that informs clinical practice in the most efficient manner, the research agenda must expand to include explanatory, pragmatic, and hybrid study designs.[41]

Explanatory trials are often conducted in a rarefied environment of free care, restricted treatment choice, specialized providers and settings, high treatment compliance, etc..[42] Pragmatic trials, on the other hand, are conducted in the messy and confounded environs of routine clinical practice. The fundamental differences between pragmatic and explanatory trials derive from their differing purposes (Table 5). An explanatory trial aims to test a biological hypothesis and ascertain whether there is a difference, whereas a pragmatic trial aims to provide evidence that will permit a choice to be made between different treatment options or policies. Thus, pragmatic trials are primarily concerned with how large the difference is.[43]

Internal and external validity are inversely related. Therefore, the two trial designs really represent different ends of a continuum separated by the degree of internal or external validity achieved in the study. At one end are explanatory trials, with high internal validity but very low external validity, and at the other end are the pragmatic trials with high external validity but compromised internal validity. Consequently, most studies are hybrid designs that fall somewhere in between.[44]

Explanatory trials are essential to the progress of medicine, but since they generally do not address questions that are of prime importance to prescribing clinicians they are not always sufficient.[45-47] Often initial studies of a novel therapy are explanatory, but once the therapy is found to have a biological effect and a safety profile that justify further study, later trials should be pragmatic and include the full range of patient types that would be likely candidates for the treatment in routine clinical practice.[43,44] However,

care must be taken to ensure that equipoise is maintained in the choice of comparator in these latter trials.

The detractors of pragmatic clinical trials are sceptical of their potentially sloppy, less sophisticated methodology because the causal link between treatment and observed clinical outcome is incrementally weakened as each element of an explanatory trial is removed.[47,48] Relaxing the rigour of a randomized controlled trial can be dangerous

Table 5: Summary of main differences between explanatory and pragmatic trials[38,43,45]

Study Characteristic	Explanatory Trials	Pragmatic Trials
Objective	Test of efficacy Tests a specific component of treatment	Test of effectiveness Tests a package of care rather than individual components contributing to that care
Inclusion/exclusion criteria	Many; narrowly defined	Few; broadly defined
Patient group	Highly selected and homogeneous	Diverse and heterogeneous Participants reflect the population for which the treatment is intended
Randomization	Usually randomization by participant	Often quasi-experimental designs with no randomization
Blinding	Often double blind	Participants blinded to treatment allocation when possible Data collectors and analysts often blinded to treatment allocation
Intervention	Standardized Simple interventions; often a discrete single activity	May be a discrete single activity, but often involves a complex intervention
Control	Often placebo-controlled	Standard care (clinically relevant interventions or no treatment)
Ancillary therapy	Forbidden	Often present Reflects clinical practice
Outcomes	Single objective, often laboratory based, outcomes	Wider spectrum; measures that are familiar to prescribing clinicians and relevant to everyday life, such as function and quality of life
Setting	Experimental setting; often larger tertiary care centre	Routine care setting
Technical skill and experience of practitioners	Usually experts	Wide variation

Table 5: Summary of main differences between explanatory and pragmatic trials[38,43,45] (cont'd)

Study Characteristic	Explanatory Trials	Pragmatic Trials
Compliance	Essential Measured to assure high level	Not essential, often low Often measured as an outcome Include non-compliers and dropouts
Sample size	Small Standard statistical determination of sample size	Large
Comorbidities	Often none	Often present
Informed consent	Lengthy	Brief
Follow-up	Usually short term	Longer term
Data collection	Limited	Extensive
Confounding	Controlled where possible	Not controlled
Internal validity	High	Low
External validity	Low	High

because it leaves the study open to bias, particularly when investigators conducting the study are enthusiastic proponents of the therapy under investigation.[49] In addition, the absence of a blinding or placebo arm can mean that the confluence of patient expectations, the Hawthorn effect, and placebo response may result in a spurious positive result. A further concern is that if patients are allowed to choose their treatment, as often happens in trials that emulate clinical practice, then any positive outcome could easily be attributed to that bias alone, particularly in the case of highly subjective outcomes such as quality of life.[48]

Pragmatic trials are, by their very nature, hard to reproduce and therefore fail one of the central tenets of science.[49] The high level of external validity often touted as an advantage in pragmatic trials can also be their downfall if the environment of the trial changes. What works today in the current healthcare milieu may not work tomorrow when such things as patient attitudes, levels of care, and service availability, all of which have been inadvertently included as part of the care 'package' under assessment, change.[49] There is also the possibility that pragmatic trials may prolong the use of treatments that are no longer effective per se, but are an innocuous component of an effective treatment package.[44] These drawbacks are a testament to the care that must be taken in designing pragmatic trials and a reminder that they are not a replacement for explanatory trials.

The increasing popularity of pragmatic clinical trials has led to speculation in the literature on ways to increase their internal validity, without sacrificing generalizability,

and make them more feasible.[13,41,45,50] These include using randomization, cluster randomization, and blinded data collection and data analysis.[45] Several alternative quasi-experimental study designs have also been suggested, including the interrupted time series; the delayed treatment design, in which all participants receive the intervention but at different times; and the regression-discontinuity design.[50] The Medical Research Council in the United Kingdom has developed guidance for designing trials of complex interventions,[51] and the European Union has recently funded Practihc (Pragmatic Randomized Controlled Trials in HealthCare), a network of 12 South African, Latin American/Caribbean, and European research institutions aimed at supporting the development and use of pragmatic clinical trials. Practihc locates and develops tools and resources for open access, and provides training and mentoring for researchers interested in designing and conducting pragmatic clinical trials.[52] It has also been suggested that a national task force comprising government, academic, provider, purchaser, and industry representatives could set methodological standards for the design and conduct of these trials.[53]

Since the environment of a pragmatic trial is all important, a description of the clinical setting or service delivery context is crucial. A further challenge is to standardize interventions while preserving usual care conditions.[42] There are accepted standards for describing and designing explanatory trials, such as the CONSORT guidelines,[54] but no such guidelines exist for pragmatic trials. Only one of the 22 CONSORT criteria addresses external validity. However, some authors have already anticipated this need by suggesting an expansion of the CONSORT guidelines to incorporate eight items on external validity.[50] Future guidelines for the reporting of pragmatic trials should be cognizant of the fact that the results of these trials will likely have a different audience to those of explanatory trials, so they should be presented in the language that clinicians, decision makers, and policy makers understand.

Issues for HTA agencies

While identifying knowledge gaps to inform the research agenda has been identified as an important future area of focus for some HTA agencies, many of the INAHTA members have yet to move beyond the stage of scoping projects. There is keen interest, but also substantial trepidation, most likely due to an awareness of the challenges in implementing such a process. Our survey of the INAHTA membership revealed a number of challenges. Many HTA agencies do not have sufficient resources, in terms of personnel and time, to commit to such a project. There is also the difficulty of providing clear explanations regarding results and valid recommendations for future research. In addition, many countries have a very well established research agenda that the HTA agencies are loathe to tamper with. The logistics of a long-term strategy are daunting, and the spectre of committing more time and money toward yet another bureaucratic process with potentially dubious results was also cited as a major disincentive.

Given this ferment of interest and inaction, it is incumbent on HTA agencies, like the AHFMR HTA Unit, that are in a favourable situation to influence the research agenda to press ahead and explore such possibilities. The potential advantages include a more rapid solution to research questions that remain unresolved after completion of an HTA, a better linkage between research proposals and funding agencies, and a more efficient use of research dollars. Similar processes have been undertaken in Belgium and the United Kingdom, but at the national level. The AHFMR pilot project is unique in attempting to apply such a process at the provincial level, where the contextualization of research questions can be maximized to ensure their relevance.

HTA has been trying for years to establish itself as a rigorous, scientific, and objective endeavour that is far removed from biased, subjective, and often misleading narrative research syntheses. Consequently, the rigid "Cochrane method" of including well-designed, randomized experimental studies in preference to quasi-experimental and case series studies has been ascendant for many years. Recently, this has relaxed somewhat with the realization that some questions are often best answered by purportedly "lower quality" research study designs. However, meticulous methods of documenting study rigour and execution are still used in an effort to quantify bias, validity, and confounding. Since the majority of the extant research gaps involve questions of effectiveness, using HTA results to formulate the most important researchable questions for funding will encourage more pragmatic clinical trials. This will force an expansion of HTA quality assessment criteria such as the GRADE approach.[55] New tools to aid HTA researchers in distinguishing between effectiveness and efficacy trials are already starting to appear in the literature.[56] Pragmatic trials that are steeped in the complexity of real life clinical practice will entail more methodological development and training in the HTA community to tackle such issues as interpreting discrepant results between explanatory and pragmatic trials and ensuring accurate synthesis of the research evidence. This task is particularly important now that HTA has a much higher profile and more people rely on HTAs as a way of digesting the volumes of sometimes contradictory research evidence produced each year.

Next Steps

Using HTA to focus research funding on areas that help clinicians and policy makers determine the best procedures for improving outcomes and minimizing costs should be a top priority for countries like Canada with universal, publicly accountable health care.[13] It is also important that the increasing willingness of healthcare decision makers to use scientific evidence is not thwarted by a lack of data.

A process was developed for distilling research gaps identified in HTAs on chronic pain management into researchable questions that a provincial research funding body, in this case the AHFMR, can use to inform its research agenda. This novel approach also identified a research team to coordinate and potentially conduct the necessary research

studies. The next step is to work with the AHFMR in establishing a formal process to prioritize the research questions, ensure that funds are allocated to answer them, and advertise the opportunity to potential researchers. A detailed review of more established programs, particularly the system in the United Kingdom, may help to inform these efforts. The HTA Unit can make this process more efficient by identifying and explicitly describing research gaps in its reports and involving clinicians, policy makers, consumers, and the public in the production of HTAs.

There are many questions and challenges ahead, both for the AHFMR and for the HTA Unit, but the process described here provides a firm base from which to move forward. The research agenda in most countries is primarily driven by hard-core researchers conducting explanatory trials. Using HTA results to identify gaps in research will encourage more balanced funding of pragmatic and explanatory trials. Like the research endeavour itself, the orchestration of such a paradigm shift will involve an incremental evolution from this tentative first step.

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APPENDIX A: SEARCH STRATEGY

Table A.1: Databases and search terms used in the search strategy

Database	Platform	Edition	Search Terms†
The Cochrane Library		Issue 2, 2006	#1 gap OR gaps OR opportunit* OR research gap* OR knowledge gap* OR information gap* OR health policy OR systematic review* OR health technology assessment* OR technology assessment* OR HTA* #2 (practical OR pragmatic) AND trial* #3 1 AND 2 "practical trial" OR "pragmatic trial"
EMBASE	Ovid	Week 1/1988 to Week 11/2006	#1 exp Professional Standard/ OR exp clinical research/ OR exp ETHICS/ OR exp Evidence Based Medicine/ OR exp Decision Making/ #2 exp Biomedical Technology Assessment/ OR exp Health Services Research/ #3 gap OR gaps OR opportunit* OR research gap* OR knowledge gap* OR information gap* OR health policy OR systematic review* OR health technology assessment* OR technology assessment* OR HTA* #4 (practical OR pragmatic) AND trial* #5 (1 AND 2) AND 3 #6 3 AND 4
PubMed	NLM	Searched 20/03/06	#1 "Ethics Committees"[MeSH] OR "Ethical Review"[MeSH]) OR "Clinical Trials"[MeSH] OR "Evidence-Based Medicine"[MeSH] OR "Decision Making"[MeSH] OR "Intervention Studies"[MeSH] OR "Research"[MeSH] #2 "Technology Assessment, Biomedical"[MeSH] OR "Health Services Research"[MeSH] #3 gap OR gaps OR opportunit* OR research gap* OR knowledge gap* OR information gap* OR health policy OR systematic review* OR health technology assessment* OR technology assessment* OR HTA* #4 (practical OR pragmatic) AND trial* #5 (1 AND 2) AND 3 #6 3 AND 4
NHS CRD		Searched 20/03/06	gap OR gaps OR opportunit* OR research gap* OR knowledge gap* OR information gap* (practical OR pragmatic) AND trial*

Note: * is a truncation character that retrieves all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc. In databases accessed via the Ovid platform the truncation character is $.

APPENDIX B: QUESTIONNAIRE USED FOR INTERVIEWING HTA RESEARCHERS

1 What was the question addressed by the report?

2 Was the report conducted in the way it was planned at the beginning?

If not, why? (Please provide a brief description)

3 What is your opinion of the quality of the studies identified by the literature search?

4 Did the selected studies address the question(s)?

5 What research and clinical issues were identified in the report?

6 What policy issues were identified in the report?

7 Are there any ongoing randomized controlled trials or clinical trials?

If yes, when do you expect the results to be published?

8 If something has been omitted or you would like to make further comments, please do so.

APPENDIX C: QUESTIONNAIRE USED FOR INTERVIEWING MEMBERS OF THE INFORMATION SHARING GROUP

1 Does this report sufficiently answer the research question(s)?

a. yes
b. no
c. partially

2 a. What are the main research and clinical questions that remain unresolved after reading this report?

b. What are the main policy questions that remain unresolved after reading this report?

Please prioritize these issues from the perspective of what are, in your opinion, the most important issues that need to be answered about this topic to improve this aspect of care/service within the Alberta health system.

3 What kind of information/data/study would best answer the unresolved issues (research, clinical, and policy), in your opinion?

4* Please identify a research group or individual(s) who would be willing to assist with designing/formulating/undertaking a research proposal to address the outstanding question(s).

Are you willing to be an active participant in upcoming research projects?

*This question was not posed to the HTA researcher

APPENDIX D: SUMMARY OF QUESTIONNAIRE RESPONSES RELATING TO THE HTA REPORT ON THE PREVALENCE OF CHRONIC PAIN[21]

1. *Does this report sufficiently answer the research question(s)?*

There was a mix of answers in relation to this question.

- The definition of non-malignant chronic pain used in the report influenced the selection of the included studies and may have been a limiting factor. **[Unanimous]**
- The HTA report only partially answered the question (the respondent did not take into account his own report on prevalence). **[Policy/HS Researcher B]**
- The HTA report, when taken in conjunction with the provincial prevalence data report, addressed the research question. **[Policy A]**
- The HTA report, when taken in conjunction with the provincial prevalence data report, only partly addressed the research question **[Clinician A, Clinician/Administrator B]**
- The research question was answered as best as it could be based on the research available. **[HTA Researcher]**

2a. *What are the main research and clinical questions that remain unresolved after reading this report?*

There were several common themes among the responses to this question.

- The definition of chronic pain and the criteria used to define it need to be standardized. Currently there is a disparate set of definitions in the research literature. **[Unanimous]**
- A scale is needed to quantify the gradations of severity within the experience of chronic pain. It would also be useful to define the severity of chronic pain in terms of both quality of life and heath service utilization. **[Unanimous]**
- The prevalence rates of chronic pain associated with various underlying pathologies, such as diabetes or migraine, where chronic pain is a symptom need to be determined. **[HTA Researcher, Clinician/Administrator B]**

- It is important to know what the prevalence is in certain population groups, such as the elderly, or males or females, and to determine what research variables, such as outcomes used and data collection methods, may affect the prevalence estimates.
  [HTA Researcher]
- There is a need to assess whether the utilization of health services changes for different diseases once chronic pain is alleviated.
  [Clinician/Administrator B]
- Prevalence is of more relevance to the bureaucrats and politicians.
  [Clinician A]

2b. *What are the main policy questions that remain unresolved after reading this report? (Please prioritize these issues from your perspective of what are the most important issues that need to be answered)*

- Policy issues were not addressed in the report.
  [HTA Researcher]
- I am not the appropriate person to answer this policy question.
  [Clinician A]
- All policy questions depend on having a prevalence rate, and this has yet not been resolved, particularly with respect to Alberta.
  [Policy/HS Researcher B]
- The threshold at which the health system should provide health services is still not known. If the severity and prevalence of chronic pain were known, the target population could be identified and the required resources allocated.
  [Clinician/Administrator B]

3. *What kind of information/data/study would best answer the unresolved issues (research, clinical, and policy), in your opinion?*

- The first step is to establish a standardized definition of chronic pain that is agreed upon by the entire pain community.
  [Unanimous]
- To the best of her knowledge, there are no ongoing studies in this area.
  [HTA Researcher]
- There is a need to establish both the prevalence and incidence of chronic pain, particularly if it is likely that either prevalence or incidence is unstable. If these rates are unstable, it is necessary to find out what risk factors, such as environmental factors, are responsible.
  [Policy/HS Researcher B]

- Prospective primary studies would be the most useful way of determining the prevalence of chronic pain in Alberta **[Clinician/Administrator B, Policy/HS Researcher B, HTA Researcher]**. Epidemiological studies using administrative data from the Health Ministry should also be included **[Clinician/Administrator B, HTA Researcher]**. Retrospective studies using chart review and linking patient data to utilization data should also form part of the study **[Clinician/Administrator B]**.
- One of the objectives of the study should be to identify the most effective way of dealing with chronic pain.
  [Policy/HS Researcher B]

4. *Please identify a research group or individual(s) who would be willing to assist with designing/formulating/undertaking a research proposal to address the outstanding question(s).*

   Are you willing to be an active participant in upcoming research projects?

   This question was not posed to the **HTA Researcher**.

   - The Information Sharing Group is a good starting point.
     [Policy/HS Researcher B]
   - The research group should include an epidemiologist, a health economist, and clinical advisors. This expertise is readily available from both the University of Calgary and the University of Alberta. I would participate in the research group.
     [Clinician/Administrator B]
   - Anyone willing to undertake such a study could do so. I do not see myself as a member of the research group.
     [Clinician A]

Summary of questionnaire responses relating to the HTA report on multidisciplinary pain programs[22]

1. *Does this report sufficiently answer the research question(s)?*

   - The report only partially answered the questions of effectiveness and efficiency of multidisciplinary pain programs **[Unanimous]**. However, this was not related to the way the HTA report was conducted, but was rather a reflection of the included systematic reviews and the approach taken by their authors **[HTA Researcher]**.
   - One respondent stated that he was not familiar with clinical efficacy data and that such a complex subject could not be completely answered by secondary research alone.
     [Policy/HS Researcher B]

2a. *What are the main research and clinical questions that remain unresolved after reading this report? (Please prioritize these issues from your perspective of what are the most important issues that need to be answered)*

There was some agreement **[Clinician A, Policy A, HTA Researcher]** on the need for multidisciplinary care to be defined in a standardized fashion, including program protocols.

- The current HTA report did not address the efficacy or efficiency of individual program components.
  [HTA Researcher]
- We need to know for which conditions these programs are cost effective, and whether multidisciplinary pain programs are more cost-effective than single interventions, such as chiropractic care.
  [Policy A]
- A cost-effectiveness study is needed that compares multidisciplinary pain programs to community care (family doctor in combination with specialty consults).
  [Clinician/Administrator B]
- There is a need to determine the effectiveness of multidisciplinary pain programs for indications other than low back and pelvic pain.
  [Clinician A, Clinician/Administrator B, Policy A]
- There is a need to define what level of service patients should receive according to their severity of pain.
  [Clinician/Administrator B]
- The current primary research is weakened because the outcome measures used were not consistent. There is a need for uniformity in how outcomes are measured.
  [Clinician A]

2b. *What are the main policy questions that remain unresolved after reading this report? (Please prioritize these issues from your perspective of what are the most important issues that need to be answered)*

- Cost is an issue **[Policy A, HTA Researcher]**. There is a lack of research data on cost utility **[HTA Researcher]**.
- There is concern that the Ministry of Health is funding chronic pain treatments that aren't supported by research evidence. In essence they thought the key question was 'is what we are funding appropriate based on what we know?'
  [Policy A]
- The respondent was apprehensive about the approach used to analyze the available research evidence since it was not designed to identify the most

effective components within a multidisciplinary pain program. In Alberta there are several multidisciplinary pain centres with programs that differ in their composition and service providers.
[HTA Researcher]

- Similar concerns were expressed regarding what types of programs work for which patient groups. There is a need to define who needs multidisciplinary pain programs (children, seniors, etc. and for what pain syndromes) and what should the program look like. For example, what specialty team mix is needed for the different levels of pain severity and for what intended impact?
[Clinician/Administrator B]
- If the previous questions were answered, a further research aim should be to develop a tool that would triage patients into different pain programs that have specific services bundled according to the patient's needs. This approach would help alleviate the current waiting lists.
[Clinician/Administrator B]
- The respondent did not feel that they were the appropriate person to answer this question but guessed that the policy questions of interest would be: how much pain is there; who is going to run these programs; and where are we going to locate them?
[Clinician A]

3. *What kind of information/data/study would best answer the unresolved issues (research, clinical, and policy), in your opinion?*

- There may be more updated Cochrane reviews forthcoming and the Institute for Work and Health in Toronto was interested in conducting an economic study. Perhaps the first step should be to conduct a systematic review that would be more robust than the previously conducted reviews, with clear selection criteria that would address some of the questions identified. Previous reviews focused only on low back pain, and there may be primary studies that deal with other pain syndromes.
[HTA Researcher]
- By conducting more HTAs there would be an opportunity to identify further 'research gaps'. The external reviewers of the HTA reports should also be approached to identify 'research gaps'.
[Clinician A]

- There is a need to conduct field evaluations of the current multidisciplinary pain programs with clearly defined research questions and standardized outcome measures.
  [Policy A]
- A comparative controlled study of multidisciplinary pain programs with community care would be helpful **[Clinician/Administrator B, Policy A, HTA Researcher]**. The study should be conducted over a minimum of five years, with follow up at six months, one year, and then annually **[Clinician/Administrator B]**.
- A comprehensive set of outcomes need to be collected that include psychological, economic, quality of life, functional, pain severity and service utilization measures.
  [Clinician/Administrator B, HTA Researcher]
- It is important to determine if the treatment effect is durable or whether regression occurs over time.
  [Clinician/Administrator B]

4. *Please identify a research group or individual(s) who would be willing to assist with designing/formulating/undertaking a research proposal to address the outstanding question(s).*

   Are you willing to be an active participant in upcoming research projects?

   This question was not posed to the **HTA Researcher**.

   - Willing to participate in the research.
     [Unanimous]
   - The Chronic Pain Information Sharing Group should be part of the research team, as well as other policy/administration people within the Health Ministry and Capital Health Region.
     [Policy A]
   - If the AHFMR provided funding for studies that are generated by questions from HTAs, more people would be willing to invest their time in providing input into HTA projects.
     [Clinician A]
   - The following expertise is needed to address the identified research questions: health economists, clinical researchers with program skills, psychologists, and community health researchers from the University of Alberta.
     [Clinician/Administrator B]

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