



American Pediatric Surgical Association

APSA New Technology Committee Innovative Therapy White Paper - 01/2014

April 27, 2016 – Approved by the APSA Board of Governors

GOAL:

The goal of this document is to offer a set of opinions/guidelines that could be used by APSA members and their institutions to inform and advise decision-making related to the introduction and establishment of new technology into surgical practice. The guidelines seek to:

- ◆ Define and differentiate Clinical Care, Innovative Therapy and Research
- ◆ Offer an evaluation and implementation framework for Innovative Therapy which encourages advances in care and technology while preserving transparency, patient safety and patient autonomy
- ◆ Offer recommendations for Innovative Therapy/Technology-specific privileging and re-privileging
- ◆ Recommend strategies for obtaining informed consent for Innovative therapy procedures

ATTRIBUTES OF INNOVATIVE SURGICAL THERAPY:

- Reflects **significant** changes in clinical procedures, technology, techniques, devices and treatment (involving more than a gradual change or “incremental variation”)
- Has not yet been introduced at the hospital, but validated elsewhere.
- Has cost implications or impact on institutional resources and and/or personnel
- Poses sufficient risk, such that that independent review would be beneficial to the patient, health care professional or hospital, particularly to prevent, and in the event of, an adverse outcome
- Provides treatment that did not exist previously (eg natural orifice transluminal endoscopic surgery)
- The proposed innovation, while expected to improve the health of a sick individual, could also place at risk, a healthy individual who would receive no direct benefit in terms of physical health from the innovation (uncertain/unknown risk profile)
- When innovative therapy differs significantly from routine clinical practice it should be viewed as “experimental”. The use of the term experimental mandates a

requirement for formal evaluation, although generally short of what would be required if the procedure was placed in the category of “research” (IRB)

- NOTE: Does not include “incremental variations” in care: An incremental variation is defined as a minor modification of a surgical procedure that is unlikely to increase risk to the patient, or significantly extend the time of anesthesia.

BACKGROUND:

Advances in medical and surgical technology have led to the development of completely novel procedures, or substantial modification of existing medical or surgical treatments. There are several recognized factors which influence surgeons and their institutions to consider the adoption of a procedure that is new or significantly modified by innovation. These include a desire to improve care and outcomes for patients, a drive to remain competitive, pressure from industry and the health care environment, and sometimes at the request of patients who specifically seek treatment with “the latest” technology.

Treatment innovation emerges at the “preclinical” or “experimental” level, (meaning that there is knowledge of its possible role in patient care, which has never been formally evaluated in humans), and continues along the knowledge translation pathway from Phase 1 and 2 clinical evaluation to formal evaluation in randomized controlled trials.

In 1979, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research created the Belmont Report, which offers a definitions which describe the boundaries between what is research and what is accepted and routine practice of medicine. At the edges of this boundary between research and clinical care is “Innovative Therapy”.

RESEARCH: A “class of activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge...that can be corroborated by accepted scientific observation or inference”. Research activities are subject to regulation by Institutional Review Boards (IRBs), which offers patients some protection against the uncertainty of the effectiveness or safety of that activity.

CLINICAL CARE (PRACTICE OF MEDICINE): “Those activities intended solely to enhance the well-being of the individual patient or subject with a reasonable expectation of success”.

INNOVATIVE THERAPY : Activities intended to benefit patients with a degree of novelty that includes the possibility of unforeseen outcomes and the possibility that generalizable knowledge about the procedure may be accumulated.

The Belmont report states: “When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is experimental in the sense of new, untested, or different does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective.”

Understanding where new therapies lie along this knowledge translation continuum helps us differentiate “research” from “innovative therapy”. “Research” is an activity designed to test a hypothesis, and permit conclusions which may be generalizable to human interventions (eg bench research). “Interventional Research” is designed to determine safety and efficacy of a human intervention by collecting data to address specific scientific questions; while there may be a potential for patient benefit, that is not

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the intent of the intervention (eg Phase 1 drug trial). Both research and interventional research are subject to IRB regulation. On the other hand, the primary objective of Innovative Therapy is to benefit the patient, and while observational data may lead to generalizable knowledge, it is not the primary intent of the intervention, and therefore need not be subject to IRB regulation.

Thus, the Belmont Report offers a framework for recognizing Innovative Therapy in Surgery, and allows for a process of review (other than IRB) whose goal is to protect the interests of patients, practitioners and institutions. This process should:

- Focus on and encourage the achievement of the highest quality surgical outcomes through innovation
- Utilize a process for introducing innovation that is transparent and publicly defensible
- Ensure that the implementation process addresses the need for prerequisite knowledge and skills of the surgeon and surgical team
- Oversee monitoring of outcomes in a prospective and preferably risk-adjusted manner for a sufficient period of time to ensure the durability of outcomes
- Assess the potential organizational impact of implementing innovative practices, especially if this results in a redeployment of resources away from other clinical areas

INNOVATIVE THERAPY AND THE FDA:

○ “FDA approved”: The FDA’s responsibility to protect public health includes its regulation of medical devices. The FDA classifies medical devices according to risk, and only highest risk devices (eg mechanical heart valves) require FDA approval prior to marketing. Prior to approval, the applicant must provide the FDA with “reasonable assurance of device safety and effectiveness”. Moderate risk devices (eg dialysis equipment and various types of catheters) may be cleared for based on an FDA determination that are “substantially equivalent” to an already legally marketed device of the same type. Low risk medical devices (eg bandages) are exempted from premarket review when they are equivalent in use and technology to existing approved products. There is little incentive within surgical device and technology markets to develop devices for specific use in children, due to their small market share. With few exceptions, the responsibility and cost of device evaluation prior to FDA approval lies with individual innovators/investors, and remains a major obstacle to surgical device development for children.

○ “Off-Label Use”: If an FDA-approved medical device is used for an indication not in the approved labelling, its use is “off-label” (alternatively referred to as “physician-directed”). Provided the physician is well-informed about the product and is using sound medical evidence to justify its use, and if the intent of use is “the practice of medicine”, then an application for request for “Investigational Device Exemption” (IDE) is not required. The institution at which the product will be used may, under its own authority, require IRB review or other institutional oversight.

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- “Investigational Use”: Investigational use implies the use of an approved product in the context of a clinical study protocol to develop information about the device’s safety or efficacy. Under these circumstances, an IDE may be required.
- “Pediatric Medical Devices”: These devices are used to diagnose and treat conditions from birth to age 21; some devices are designed specifically for children, while others are adapted directly from adult applications. The FDA recognizes the market challenges of designing medical devices for children, and has developed initiatives to support the development of safe and effective pediatric medical devices. These include the Pediatric Device Consortia Grant Program, and the FDA Office of Orphan Products Development. Both offer grant programs for funding clinical research related to pediatric device development. The Humanitarian Use Device (HUD) Program permits an alternate pathway to FDA approval for a medical device that targets a disease or condition that affects fewer than 4,000 individuals in the US per year.

Despite the role of the FDA in approving surgical devices, it is important to realize the FDA’s limited oversight role for surgical innovation in children. As discussed below, the primary responsibility for ensuring that innovation is introduced safely and with transparency, lies with the treating surgeon, working collaboratively with a committee tasked with the critical appraisal, approval and oversight of proposed innovative surgical procedures.

EVALUATION OF PROPOSED INNOVATIVE SURGICAL THERAPY:

A submission of a proposed therapy for adjudication as Innovative Therapy should address the following questions:

- Is there evidence supporting its safety and effectiveness?

Evidence of safety and effectiveness is often difficult to find in evaluating new technology. If the technology is new and approved by the FDA, the approval process provides some assurance. If the innovation represents application of existing technology to a new clinical problem or patient population, hypotheses regarding safety and effectiveness in another clinical situation can be made, but definitive proof is unlikely to exist.

- Is the proposed innovation technology or patient care driven?

There are several intrinsic and extrinsic forces that may be influential of decisions to implement or not implement a novel surgical technology. These may include the appeal of new technology, the surgeon’s or institution’s desire to be seen as “cutting edge” in a competitive healthcare environment, and even pressure from patients who are actively seeking care that uses the newest technology. Ultimately, a desire to provide safe care to patients which offer improvements in outcome over what is currently available must be the overarching goal

- How will surgeon and surgical team training be accomplished, and how will post-privileging performance be monitored

This is a critical step in the process which considers the following foundational elements: Education, Objective assessment of acquired knowledge and skills, graduated levels of complexity as the team acquires experience, procedure-specific

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outcomes monitoring along the learning curve and afterwards. The experience with CBD injury in laparoscopic cholecystectomy is an example of what can happen when this iterative process is bypassed.

- Does a real or perceived conflict of interest exist with any member of the surgical team or the institution?

This is a potentially “slippery slope”. If an implemented new technology is shown to be safe and effective, then early adopters have a professional obligation to become responsible advocates for its use. However the role as “responsible advocate” must always be primarily for the benefit of patients, and there is a real/perceived threat to that role if other potential influences, (especially financial) are not openly disclosed.

- What is the likely cost impact?

A thorough “business case” for implementation to estimate its fiscal impact is recommended. In addition to the capital investment required, there are often operational budget implications, that include “costs per case” (especially if the procedures are lengthier, or use disposable instruments), which may be potentially offset if the patient outcomes include reduced lengths of stay, or if patient volumes are likely to increase due to the specific availability of the procedure, or from the salutary benefit of “innovation” on the hospital’s ability to increase its patient base.

- Should the proposed innovative therapy be subject to an IRB-approved research protocol?

A new procedure or emerging technology for which there is no published evidence in support of its safety and effectiveness, should be implemented in the context of an IRB-approved trial. In rare circumstances, a situation may arise in which standard approaches have failed, or no standard treatment alternative exists, and there is an element of urgency in the required treatment. Under such circumstances it may be appropriate to use an innovative treatment on compassionate grounds, despite a lack of clear evidence of its safety or effectiveness. It is recommended that a hospital ethics committee be engaged in such a decision, and the consent process must clearly indicate that an innovative treatment is being offered on compassionate grounds, without clear evidence that it will be effective.

THE APPLICATION PROCESS:

The process includes a written application that includes the following information:

1. A description of the procedure
2. Summary and characterization of evidence of effectiveness and safety of procedure (pediatric evidence > adult evidence > experimental evidence)
3. Evidence of endorsement by procedural experts outside the institution
4. Summary of potential risks and benefits to patients
5. Declaration of real or perceived conflicts of interest

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6. Number of patients to be treated during the “Approval Period”
7. Expected impact (positive and negative) on resources: device costs, procedural time, LOS, etc.
8. Signature of the responsible financial director (indicating awareness of the proposal and availability of appropriate resources)
9. Assurance of device approval for use in patients (FDA, Health Canada)
10. Assurance of appropriate expertise/training of the surgeon and team (including education plan, preceptorship/ proctorship)
11. Outcomes monitoring plan

GOVERNANCE:

Chief of the Clinical Division from which the request originates, plus one or two invited members not usually involved in the care of these patients (Surgeon in Chief, Clinical leader in Anesthesia or Pediatrics). This group assembles the Review Team for the specific innovative therapy request.

CREDENTIALING, PRIVILEGING and MAINTENANCE OF PRIVILEGES:

Once a decision has been made to implement a new surgical technology to a hospital’s operating room, a sequence of steps should follow, which preserve patient safety and optimal clinical outcomes as the highest common goal.

- 1) Who (and how many) should be trained?

There are likely to be local factors that determine who should be trained. There may be surgeons who are already experienced in innovation (eg laparoscopic surgery) who might be obvious choices. The number to be trained should be informed by historical or projected case volumes, since maintenance of skills will be determined by annual case experience. Recommendations vary, but the experience with robotic surgery suggests that skills maintenance requires performance of a minimum of 20-24 cases per year.

- 2) What are the Credentialing requirements?

- Documentation of general knowledge and procedural competency related to the condition to be treated by the proposed procedure must be documented. One obvious prerequisite is successful completion of a residency/fellowship training program for which treatment of the proposed condition is a core competency. An accepted proxy for competency is Board Certification by a recognized oversight group (eg ABS). The hospital’s compliance with regulatory agencies such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) should offer assurance that the practitioner has basic knowledge and procedural competency for initial and renewal privileging, but does not address the need for specific knowledge and skill required to grant privileges for an innovative procedure

- 3) What are Privileging Requirements?

- Documentation of specific knowledge related to the technology itself. Whether the innovation represents a procedure, technique, or device there should be

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documentation of knowledge related to the proposed innovation, including training /troubleshooting in the use of new equipment, a full understanding of procedural indications and contraindications, an awareness of unique intraoperative, postoperative complications related to the procedure/device and knowledge of the steps necessary to manage those complications, and an awareness of the importance of monitoring patient outcomes after the procedure has been introduced into clinical practice.

- Acquiring and documenting Innovative Surgical Skills: Standardized educational programs which emphasize a “disease-based” rather than “technology-driven” approach should be used. Courses should be accredited by a professional oversight organization (eg American College of Surgeons Accredited Education Institutes) or by professional societies (eg American Pediatric Surgical Association, Society of American Gastrointestinal and Endoscopic Surgeons). These courses must have clear objectives, be contextually relevant and interactive, and emphasize the stepwise learning of component tasks through detailed task analysis. Models or simulators of varying fidelity can be used to assist in the teaching, learning and assessment of surgical skills. Depending on procedural complexity, there may also be the need for formal team training in roles and situational awareness, with use of checklists, and procedural rehearsals.
- Preceptoring and Proctoring: *Preceptors* are local or national experts who serve as teachers or coaches, and conduct assessments of the learner’s skills using valid tools. Preceptors must be a procedural or technology expert. They typically assist in the performance of the operation and are able to assume primary responsibility should the need arise. Preceptors require surgical privileges in the facility in which they are assisting, and may be exposed to legal risk should an adverse event occur. *Proctors* play a primary role in the verification of a learner’s knowledge and skills while they are still on the steep portion of their learning curve, and provide reports that can be used to grant privileges. Their role is to observe and provide feedback to the learner. Although desirable, they need not be an expert in the performance of the procedure, and their presence at an operation, as an observer, is not associated with legal risk. There should be a requisite number of proctored cases (average 2-4) prior to a surgeon becoming credentialed for that procedure or technology.

4) Privileges have been granted for an Innovative Procedure. What now?

- Undertake simple cases before complex ones. If the technology is adaptable to both simple and complex operations, then simple cases should be scheduled first to acquire experience with the technology.
- A minimum number of cases (at least 5) at the beginning of the experience should be subject to focused review, which considers procedure-specific outcomes, including complications, blood loss, conversion to a traditional operative approach. A surgeon/surgical team whose performance does not meet a competency threshold (usually based on published standards or historical outcomes with the traditional technique) has the option of obtaining additional training, then undergoing re-proctoring and followup competency evaluation. Ultimately, a failure to achieve competency targets should result in a withdrawal of privileges for that procedure.
- Navigating the learning curve during early surgical/surgical team experience with innovative therapy. The learning curve (defined as the number of procedures required for a surgeon or team to achieve optimal performance as measured by procedural time, patient outcomes) varies substantially between procedures. While the team is

progressing along its learning curve, consideration should be given to a “second timeout” a few hours into the procedure, to allow the operative team to refocus on patient safety goals. The learning curve outcomes, especially procedural time, blood loss, and complications should be monitored

- Maintenance of privileging through annual minimal case numbers and satisfactory patient outcomes. Based on recommendations from robotic surgery, a surgeon should perform a minimum of 20 robotic procedures per year. For technology applied to more than one procedure (especially if the individual procedural frequency is rare), it may be reasonable to “bundle” like procedures as a means of meeting annual volume targets. Development of standardized outcomes (preferably with some patient risk adjustment) reported in a “balanced scorecard” format is a potentially useful means of conducting ongoing post-implementation evaluation

PROTECTION OF PATIENTS RECEIVING INNOVATIVE THERAPY:

1. Accurate portrayal of risks and benefits of Innovative Technology

- Hospital websites as “Sources of Truth”. There is evidence that patients search the internet for reliable information for “state of the art” care, and that hospital websites are considered sources of information that are accurate and trustworthy, and that the content posted on a website is “a physician’s voice”. There are few regulations governing what hospitals can report regarding quality of care on their websites, hence the potential for misinforming patients through inaccurate portrayal of the risks and benefits of innovative therapy exists. There is already good evidence that this occurs with robotic surgery with direct use of manufacturer-provided materials on hospital websites and unjustified claims of clinical superiority (less pain, shorter recovery, reduced blood loss and improved cancer outcomes), with no citation of any supportive data, and no mention of the specific risks associated with robotic surgery.

- Adverse Events Reporting. Clearly defined processes for reporting adverse events or malfunctions following regulatory approval of new devices exist. Transparency and accuracy of reporting is critical, as it enables accuracy in risk assessment by patients and the medical community, and it directly informs future regulatory agency approval of devices for other uses (eg FDA clearance of use of DaVinci robot for pediatric surgical procedures in 2005, after initial approval for general surgical procedures in 2000). Recent evidence suggests that robotic surgery complications have been underreported to the FDA, both by physicians reporting to the manufacturer and by the manufacturer to the FDA.

- Other mechanisms for early detection of clinical outcomes associated with Innovative Procedures. In addition to adverse events, the quality of clinical outcomes informs whether new procedures should be adopted as a standard of care. When the numbers of patients treated at single institutions is small, the creation of a patient registry (eg International STEP registry) with standardized outcomes reporting, allows a more rapid determination of clinical effectiveness of new procedures.

2. What are the key elements of an informed consent in a patient undergoing innovative therapy to ensure autonomy of decision-making?

- Patients must be made aware that a procedure is innovative and be advised of procedure-specific adverse outcomes. They should be informed of the known benefits and risks of the proposed procedure and of the alternate “proven” procedure. Patients

should be provided with some information regarding the experience of the surgeon/team with the innovative procedure, and the learning curve implications. These points must be addressed and documented (preferably in writing) in the informed consent process for innovative procedures.

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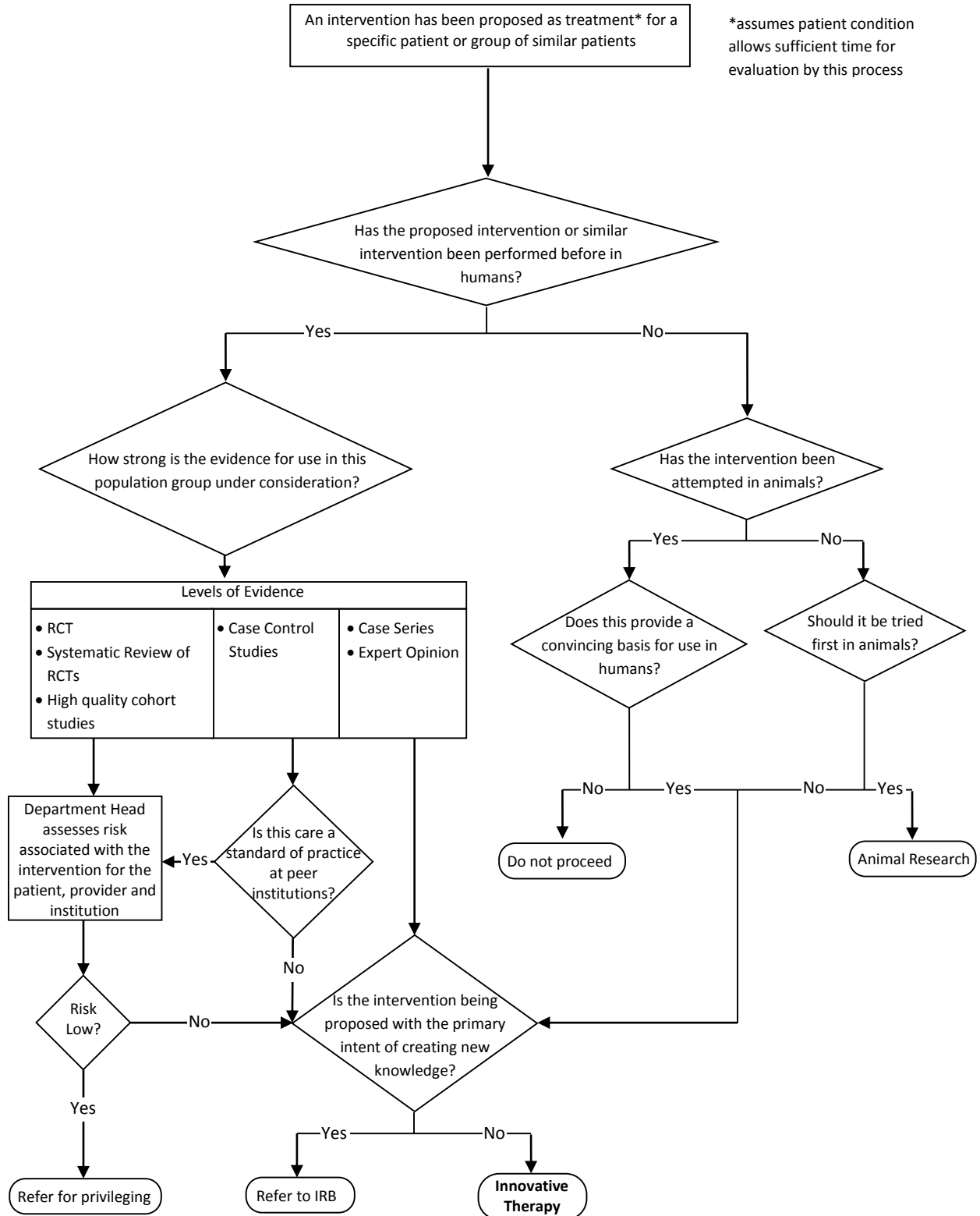
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Figure 1:

Differentiating Clinical Care, Innovative Therapy and Research



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Figure 2:

