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SPECIAL REVIEW – EVIDENCE BASED CARDIOLOGY

Health technology assessment (HTA) in cardiac field

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1. Introduction

Rapid developments in new health care technology in the cardiac field have become almost daily events. The technological development involves a wide range of applications of diagnostic modalities such as cardiac MRI, PET, CT angio or genetic screening for cardiac risk factors. It also covers countless therapeutic interventions, e.g., new anti-platelets, new pulmonary vasodilators, implantable cardioverter-defibrillators (ICD) drug-eluting stents, off pump coronary bypass, ventricular assist devices and robotic surgery. The term "technology creep" describes a phenomenon in which a certain technology first gets approved for a high-risk population in which there's a proven benefit and its use then expands to lower-risk groups, changing the calculus of clinical and financial risk and reward. The ICD was first used for people who had survived cardiac arrest and are now "*recommended*" for primary prevention in patients with low ejection fraction (Epstein et al., 2008). The estimated cost per QALY for each device ranges between $50,300 and $70,200 (Health Technol Assess, 2006). Cardiac centers compete to attract doctors and patients by buying advanced tools. If Hospital A has a PET scanner and cardiac MRI and Hospital B does not have them, Hospital B loses in reputation and volume. This is regardless of the degree of need or priority of the presence of these technologies in certain community.

Unfortunately, adopting these new technologies can put a huge burden in the health systems costs. The annual medical cost of a CVD in USA is exceeding $403.1 billion (Patel and et al., 2005). This is true not only at the individual patient management but also at the nationwide level decisions to adopt such technology. Since available resources are limited, delivering health services involves making decisions. Decisions are required on what interventions should be offered, the way the health system is organized, and how the interventions should be provided in order to achieve an optimal health gain with available resources, while, at the same time, respecting people's expectations.

2. Health technology assessment (HTA) as a continuum of evidence-based medicine (EBM)

The practice of EBM depends on the strength of evidence (level of evidence) and strength of recommendation (grade of

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Evidence Based Medicine is as simple as 1-2-3-4-5

1. MAJOR AIM	Best patient's Care
2. MAJOR PRINCIPLES	Evidences are not equal (evidence hierarchy) are not enough (the 3 Es)
3 .COMPONENTS	3 Es Evidence- Expertise-Expectations
4 .PILLARS for appraisal	RVRA system Relevance-Validity-Result clinical significance-Applicability
5.STEPS	5 As • Assess your patient • Ask structured answerable clinical questions • Acquire the best evidence • Appraise the Evidence • Apply the best Evidence

Figure 1 EBM concepts.

recommendation). This practice is based on two types of analyses which are analysis of evidence and analysis of outcome. The HTA process can be considered as an extension of the EBM process with the addition of two more types of analyses which are value analysis (cost/effectiveness) and appropriateness analysis (ethical–legal and societal). These dimensions are shown in Fig. 4.

2.1. Stage of evidence analysis – quality of evidence

The newest isn't always ''the best,'' and the latest isn't always the right answer. It is now clear that interventions once thought to be beneficial have, in the light of more careful evaluation, turned out to be at best of no benefit or harmful and counterproductive to the system. The famous hormonal replacement therapy HRT ''recommendation'' was adopted to reduce cardiac risk in postmenopausal females based on several observational studies. Later after better research quality by RCT in Women's Health Initiative (2002), this recommendation proved to be harmful. This illustrated the importance of practicing ''Evidence-Based Medicine or EBM,'' which argues that the information should be based on rigorous research to the fullest extent possible (Guyatt and et al., 2008). Fig. 1 shows the major concepts of EBM and the concept of best available evidence. This concept implies a ''hierarchy'' of evidence. Since the evidence comes from research, it is important to consider (Fig. 2):

1. The hierarchy of research designs.
2. The quality of the research execution.

Some research studies are considered to be better than others. Evidence from good research is considered to be better than evidence resulting from research of a lesser standard. This was very clear in HRT trials. The first is an evidence analysis—a systematic evaluation of evidence for a technology and a requirement of good evidence for such things as coverage, placement on formularies, and affirmative guidelines. This stage corresponds to the evidence-based guidelines (EBGs) part of EBM.

2.2. Stage of outcome analysis – grade of recommendation and benefit/risk ratio

In general the strength of recommendations is related to the strength of evidence and it was accepted that strong evidence

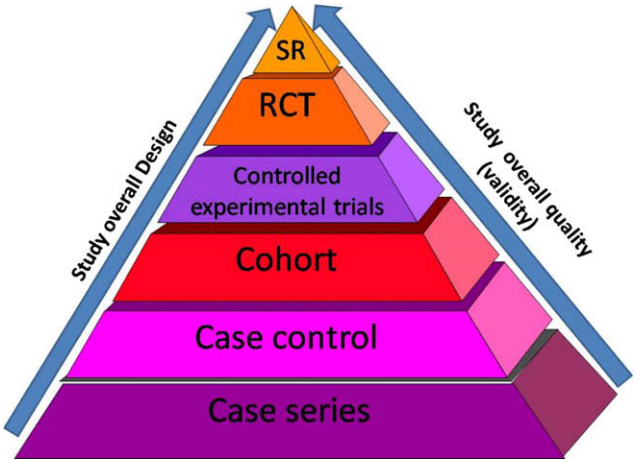

Figure 2 Hierarchy for level of evidence (in intervention).

on the effects of an intervention (positive or negative) allows for strong recommendations for or against the use of it. Weak evidence only supports weak recommendations. For several years, many systems established to link between the strength of the evidence and the grade of recommendation and typically using letters (for instance A, B, C, etc.) to describe the strength of a recommendation. Over the last two decades it has been realized that a recommendation based on the two elements of study design and validity frequently is inadequate. The GRADE system suggests that study quality should go beyond validity to include other factors that can increase or decrease its overall quality. In addition to the presence of any type of bias (that reduces the validity), GRADE considered other factors that if present should reduce the quality namely inconsistency, impression, indirectness and small magnitude of effect.

On the other hand, GRADE considered the presence of certain factors (beyond validity) should increase the overall quality (namely; presence of dose–response, strong association or all plausible confounders would result in an underestimate of the treatment effect). The major addition of the GRADE system is in its methodology in moving from evidence to recommendation. Since interventions may have both positive and negative effects at the same time, GRADE system proposed a framework to make explicit the trade-offs between harms and benefits (GRADE Working Group, 2004). Fig. 3 shows a diagram explaining the GRADE system. The second stage of outcomes analysis is an estimation of the magnitude of the effects of the technology on the desired clinical outcomes (the ''benefits'') and on potential harms such as side effects and risks (the ''risks''). This stage also includes a comparison of benefits and risks, to determine if the ''benefit–risk ratio'' is sufficiently high to justify the technology.

2.3. Stage of value analysis

Here the researcher estimates the effect of the technology on costs and compares the clinical effects against the costs to determine if the ratio is sufficiently high. In this stage there will be cost analysis and cost-effectiveness analysis. If this is combined with the previous two analyses then a decision tree can be plotted. The decision tree basically is a plot that contains the various treatment options with the calculation of two factors (a) probability factor and (b) utility (or disutility) factor.

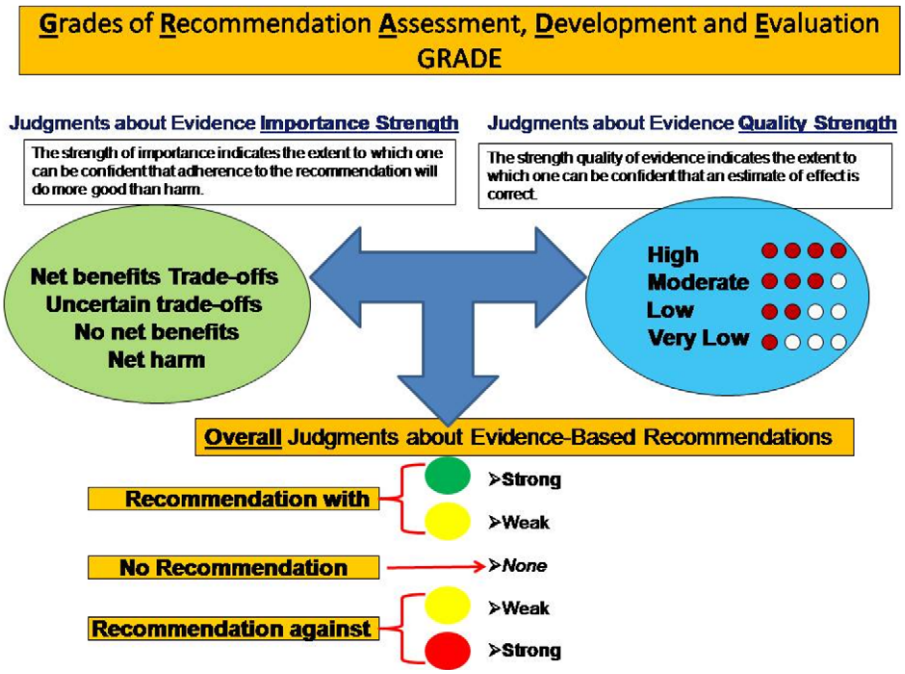

Figure 3 GRADE system.

The probability factor expresses (through evidence analysis) the probability of having an outcome with this treatment option. While utility/disutility factor expresses the value of the outcome either by its costs/cost-effectiveness or by patient values and preferences for this outcome. From this tree a decision can be made to adopt or decline certain type of intervention on an individual patient case scenario (Guyatt and et al., 2008).

2.4. Stage of appropriateness analysis (ethical–legal and societal)

The adoption of the technology frequently (if not always) requires careful assessment not only the effectiveness of such technology and its risk/benefit balance, but also other ethical, social and economic factors. It is logical that the effectiveness of a particular technology constitutes the core component in making a decision to adopt this technology. However, other key factors should contribute to such decision such as the appropriateness of this technology, its feasibility, its legality, the patient access to it and its impact on the health system and the society as a whole. This requires a complex type of appropriateness analysis that may involve in some occasions qualitative type of research. RAND Corporation developed well structured methods for establishing appropriateness called RAM (Rand Appropriateness method) that is widely used in European countries (RAND). Ethical consideration arise in HTA in the form of normative concepts (e.g., valuation of human life); applications of technology (prevention, screening, diagnosis, therapy, etc.); research and the advancement of knowledge; allocation of resources. The equity in accessing the medical technology also contributed in raising multiple ethical questions regarding certain technologies.

As denoted in the literature (David Eddy, 2009) the methodological progression of these stages is apparent. One cannot estimate the magnitude of clinical outcomes (stage 2) without first evaluating the clinical evidence (stage 1). One cannot compare the costs and cost-effectiveness (stages 3) without estimating the effects on the clinical outcomes (stage 2). One cannot think about ethical and legal implications of the technology (stage 4), until one knows something about the costs. These stages are not only ordered methodologically, they are also ordered in terms of their political and social acceptability. Until very recently the appropriateness of a technology was determined pretty much by whatever physicians wanted to do. No further information was needed. From the point of view of physicians and patients, this is clearly a highly desirable "methodology" for determining the coverage of a technology. It puts virtually no restrictions on what can be done or paid for. Furthermore this method has prevailed for hundreds of years. People are not only used to it, they are addicted to it. The first stage of a HTA, the analysis of evidence, is not only younger (about 20-years old) but considerably more restrictive. It says that before a physician can do something there must be a systematic evaluation of evidence, and only those things that are supported by good evidence will be paid for. The second stage, which calls for estimating and comparing the magnitudes of benefits and harms, is even more restrictive. It implies that there is some threshold beyond which even effective treatments might be denied if the benefit risk ratio is considered too small. Finally, an explicit consideration of costs is the most restrictive of all. It explicitly states that effective technologies can be denied if they are deemed to cost too much. In societies where for decades few have had to pay directly for their health care, this is the most obnoxious of all. So the fact that HTA programs in different countries have progressed to different stages reflects not only methodological concerns but social and political concerns as well. The fact is that different countries have reached different stages in their social and political acceptance of the different parts of an HTA. Correspondingly, the HTA programs in different countries have reached

different stages. In many settings the profession and the public are not ready for full HTAs and the difficult choices (rationing) they imply. Given the strengths of the methodologists working around the world, it is almost certainly these social and political constraints, and not the resource or methodological constraints that have caused different programs to get stuck at different phases in their HTAs (David Eddy, 2009).

3. Definition of HTA

According to the International Network of Agencies for Health Technology Assessment (INAHTA), HTA is a multidisciplinary field of policy analysis. It studies the medical, social, ethical, and economic implications of development, diffusion, and use of health technology (INAHTA). This definition implies a wide array of research that goes beyond effectiveness. Health technology assessment is the systematic evaluation of properties, effects or other impacts of health technology. The main purpose of HTA is to inform policymaking for technology in health care, where policymaking is used in the broad sense to include decisions made at, e.g., the individual or patient level, the level of the health care provider or institution, or at the regional, national and international levels. HTA may address the direct and intended consequences of technologies as well as their indirect and unintended consequences. HTA is conducted by interdisciplinary groups using explicit analytical frameworks, drawing from a variety of methods.

HTA can be used in many ways to advise or inform technology-related policymaking. Among these are to advise or inform:

- Regulatory agencies about whether to permit the commercial use (e.g., marketing) of a drug, device or other technology.
- Health care payers, providers, and employers about whether technologies should be included in health benefits plans or disease management programs, addressing coverage (whether or not to pay) and reimbursement (how much to pay).
- Clinicians and patients about the appropriate use of health care interventions for a particular patient's clinical needs and circumstances.
- Health professional associations about the role of a technology in clinical protocols or practice guidelines.
- Hospitals, health care networks, group purchasing organizations, and other health care organizations about decisions regarding technology acquisition and management.
- Standards-setting organizations for health technology and health care delivery regarding the manufacture, use, quality of care, and other aspects of health care technologies.
- Government health department officials about undertaking public health programs (e.g., vaccination, screening, and environmental protection programs).
- Lawmakers and other political leaders about policies concerning technological innovation, research and development, regulation, payment and delivery of health care.
- Health care product companies about product development and marketing decisions.
- Investors and companies concerning venture capital funding, acquisitions and divestitures, and other transactions concerning health care product and service companies.

Three basic orientations to HTA are as follows:

- *Technology-oriented* assessments are intended to determine the characteristics or impacts of particular technologies. For example, a government agency may want to determine the clinical, economic, social, professional, or industrial impacts of population-based CAD screening, or other particular interventions.
- *Problem-oriented* assessments focus on solutions or strategies for managing a particular problem for which alternative or complementary technologies might be used. For example, clinicians and providers concerned with the problem of diagnosis of CAD and DM may call for the development of clinical practice guidelines involving some combination or sequence of clinical history, clinical examination, and diagnostic imaging using various modalities.
- *Project-oriented* assessments focus on a local placement or use of a technology in a particular institution, program, or other designated project. For example, this may arise when a hospital must decide whether or not to purchase a magnetic resonance imaging (MRI) unit, considering the facilities, personnel, and other resources needed to install and operate an MRI unit; the hospital's financial status; local market potential for MRI services; competitive factors; etc.

3.1. Value vs. cost

As an example, in HTA of the value of different strategies for managing end-stage heart failure, Table 1 illustrates (Hogness and Van Antwerp, 1991) that, although the cost of conventional medical treatment is the lowest, its value per QALY is the highest, as the life-years gained and the patient utility of those years are low compared to the alternatives. The costs of heart transplantation and total artificial heart are of similar magnitude, but the value per QALY is much lower for heart transplantation, as the life-years gained and the patient utility of those years are higher compared to the total artificial heart.

3.2. HTA and underused technologies

When used properly, HTA can reduce or eliminate the use of technologies that are not safe and effective, or whose cost is too high relative to their benefits. As discussed above, HTA can also be used to remove technologies from the market that are harmful or ineffective. On the other hand HTA can identify technologies that are underused, and to help determine why they are underused. Some of the intervention that was recognized to be underused in US despite its proven value (McGlynn et al., 2003) is shown in Table 2.

3.3. Conflict of interest

HTA should consider the potential for conflict of interest on multiple levels. One is on the part of investigators who conducted and reported on the clinical trials and other studies that comprise the body of evidence under review. A second is on the part of sponsors of the primary research, e.g., technology companies, who have varying degrees of control over what research is conducted, selection of intervention and control treatments, selection of endpoints and follow-up periods, and

Table 1 Cost and value for alternative therapies for end-stage heart disease (Hogness and Van Antwerp, 1991).

Therapy	Life-years gained (year)	Mean utility	QALY (year)	Aggregate cost ($)	Cost per QALY ($/year)
Conventional medical treatment	0.50	0.06	0.03	$28,500	$950,000
Heart transplantation	11.30	0.75	8.45	$298,200	$35,290
Total artificial heart	4.42	0.65	2.88	$327,600	$113,750

Table 2 Underused health care technologies (US) (McGlynn et al., 2003).

ACE inhibitors for treatment of heart failure
Beta blockers for survivors of acute myocardial infarction
Cholesterol-lowering drugs for patients at risk of coronary artery disease
Implantable cardioverter-defibrillators for survivors of cardiac arrest
Smoking cessation interventions
Warfarin to prevent strokes due to atrial fibrillation

whether research results are submitted for publication. Another is on the part of the health technology assessors themselves, including analysts, panel members, or other experts involved in reviewing the evidence and making findings and recommendations (Bekelman et al., 2003).

3.4. Horizon scanning

The demand for scanning of multiple types of sources for information about new health care interventions has prompted the development of "early warning" or "horizon scanning" functions in the US, Europe, and elsewhere (Douw et al., 2003). Horizon scanning functions are intended to serve multiple purposes, including to:

- Identify potential topics for HTA and information for setting priorities among these.
- Clarify expectations for the uses or indications of a technology.
- Increase public awareness about new technologies.
- Estimate the expected health and economic impacts.
- Identify critical thresholds of effectiveness improvements in relation to additional costs, e.g., to demonstrate the cost-effectiveness of a new intervention.
- Anticipate potential social, ethical, or legal implications of a technology (Harper et al., 1998).

3.5. Moving from sporadic assessment to formal HTA

Even though a formal HTA programme might not be in place in a given country, decision-making about the adoption of new technologies may be part of the operational routine of health authorities and health service providers (Deyo, 2002; Hoffman, 2002). Decisions, however, are frequently based on unilateral industry information, particular interests of individuals or "gut feelings." At best, decisions take into account experience generated in other countries or selective expert advice. The challenge is to shift to a decision-making process that follows modern principles such as Evidence-Based Medicine (EBM), cost-effectiveness and patient centered services. Moving to a formalized and systematic HTA program requires a solid commitment from governmental authorities and a designated and motivated team of professionals that take charge of the HTA development plan. The establishment of one formal "HTA Agency" should not necessarily be the sole focus when targeting the creation or upgrading of national "HTA capacity." Quite often the establishment of a structured HTA network integrating existing national institutions and steered by an HTA commission (or HTA co-ordination board) is a more appropriate solution (Lehoux et al., 2005).

4. Dissemination plan

NIH proposed few approaches for HTA report dissemination.

4.1. Target groups

- Clinicians (individuals and specialty/professional organizations).
- Patients/consumers (individuals and organizations).
- Provider organizations (hospitals, clinics, and managed care organizations)
- Third party payers (government and private sector).
- Quality assurance and utilization review organizations.
- Government policymakers (international, national, state, and local).
- Biomedical researchers.
- Health care product companies.
- News professionals (popular and scientific/professional journalists and editors).
- Educational institutions (schools and continuing professional education programs).

4.2. Media

- Printed: direct mail, newspapers and popular journals, scientific/professional journals and newsletters, posters, pocket cards.
- Electronic: internet, television, radio, video disks, computer databases (online and disk).
- Word of mouth: informal consultation, formal lectures and presentations, focus groups.

4.3. Implementation techniques or strategies

- Patient-oriented: mass media campaigns, community-based campaigns, interaction with clinicians (including shared decision procedures and interactive video disk), modify insurance coverage (more or less generous benefits and change copayments).
- Clinician-oriented: conferences and workshops; continuing professional education; professional curriculum development; opinion leaders; one-on-one educational visits ("academic detailing"); coverage/reimbursement policy;

precertification; mandatory second opinion; drug formulary restrictions; feedback (e.g., on laboratory test ordering relative to criteria/guidelines); reminder systems (e.g., as part of computer-based patient record systems); medical audit/peer review; criteria for board certification/recertification, state licensure, Medicare PRO action, specialty designation, professional/specialty society membership; public availability of performance data (e.g., adjusted mortality rates for certain procedures); defense against sanctions and malpractice action.
- Institution-oriented: accreditation, standards (e.g., hospital infection control and clinical laboratories), benchmarking, public availability of performance data.

5. Decentralization of HTA

Although technology assessment originated as a primarily centralized function conducted by federal government agencies or other national- or regional-level organizations, HTA has become a more decentralized activity conducted by a great variety of organizations in the public and private sectors that make technology-related policy decisions. As noted above, an HTA done from a particular perspective may not serve the technology-related policymaking needs of other perspectives. Even for the same technology or clinical problem, there can be widely different assessment needs of politicians, regulatory agencies, health technology companies, hospitals, payers, physicians, and others. These needs are heightened with increased economic responsibilities and pressures on these different parties.

Increasingly, large health care providers and major health care product companies are establishing units devoted to "technology assessment," "pharmacoeconomics," "clinical effectiveness," "health outcomes research," and related areas. More health plans (including various managed care organizations and insurance companies) have established formal programs to assess new procedures and other technologies in support of payment decisions. The number and magnitude of private firms and university centers involved in HTA is increasing. HTA committees (with various names) are now common among medical specialty and subspecialty societies. Hospital networks, managed care organizations and other large health care providers in the private sector have HTA programs to support acquisition and management of pharmaceuticals (e.g., P&T committees), equipment and other technologies and other technology-related needs throughout their systems (Kaden et al., 2002).

The nature of an assessment problem will affect the determination of the most appropriate organization to conduct it. Certainly, a comprehensive HTA addressing multiple attributes of a technology can be very resource intensive, requiring considerable and diverse expertise, data sources, and other resources. Some health care organizations, such as some ministries of health and national health services, major insurance companies, health plans, and integrated health systems, have their own internal HTA programs. For example, in a large hospital or health plan, this might include a core staff and a multidisciplinary HTA committee representing major clinical departments, nursing, pharmacy, allied health, biomedical engineering. This committee might interact with other committees such as pharmacy and therapeutics ("P&T"), strategic planning, and capital planning committees. Other organizations rely on assessment reports acquired from organizations that have devoted functions or otherwise specialize in HTA.

Health care decision makers can "*make or buy*" HTAs. Determining the responsibility for sponsoring or conducting an assessment depends upon the nature of the problem, financial resources available, expertise of available personnel, time constraints, and other factors. For any assessment problem, an organization must determine the extent to which it will devote its resources to conducting the assessment itself or purchasing it from other sources. Some health care organizations commission selected components of an HTA, such as evidence retrieval and synthesis, and perform the other steps in-house.

One of the potential advantages of requesting or commissioning an outside group to conduct HTAs is to gain an independent, outside view where a requesting agency might have a perceived conflict of interest. Thus, a major health care payer might seek an HTA from an outside group to inform its coverage decision about a costly new technology in order to diminish perceptions of a potential bias against making a decision not to cover the technology (NIH).

6. Barriers to HTA

Although the general trend in health care is toward wider and improved HTA, several countervailing forces to HTA remain. Foremost, particularly in the US and other wealthy countries, has been a "technological imperative" comprising an abiding fascination with technology, the expectation that new is better, and the inclination to use a technology that has potential for some benefit, however marginal or even poorly substantiated (Deyo, 2002). Some argue that the increased potential of technology only raises the imperative for HTA (Hoffman, 2002). Another countervailing factor is the sway of prestigious proponents or a "champion" of a technology in the absence of credible evidence. A third impediment is the inertia of medical practice, e.g., in the form of reluctance to change long-standing practice routines, conservative payment policies, and quickly outdated education. This is complemented by lack of opportunities for, or encouragement of, scientific inquiry and skepticism in clinical education.

Ever more effective marketing and promotions, including short courses sponsored by medical product companies to train physicians in using these products, can divert attention from key concerns of HTA. Another obstacle is the limited level of investment, by government and industry sources in HTA and related evaluations of what works in health care. Although some assessment programs and certain HTA findings are nationally or internationally recognized, the resources allocated for HTA in the US are virtually lost in the rounding error of national health care expenditures. Finally, the impression persists in some quarters that the goal of HTA is to limit the innovation and diffusion of health care technology (NIH).

7. Chain of EBM–HTA

In summary, every HTA begins with an evaluation of the evidence for the technology being assessed. In that sense EBM and HTA constitute a continuum. EBM itself has two parts

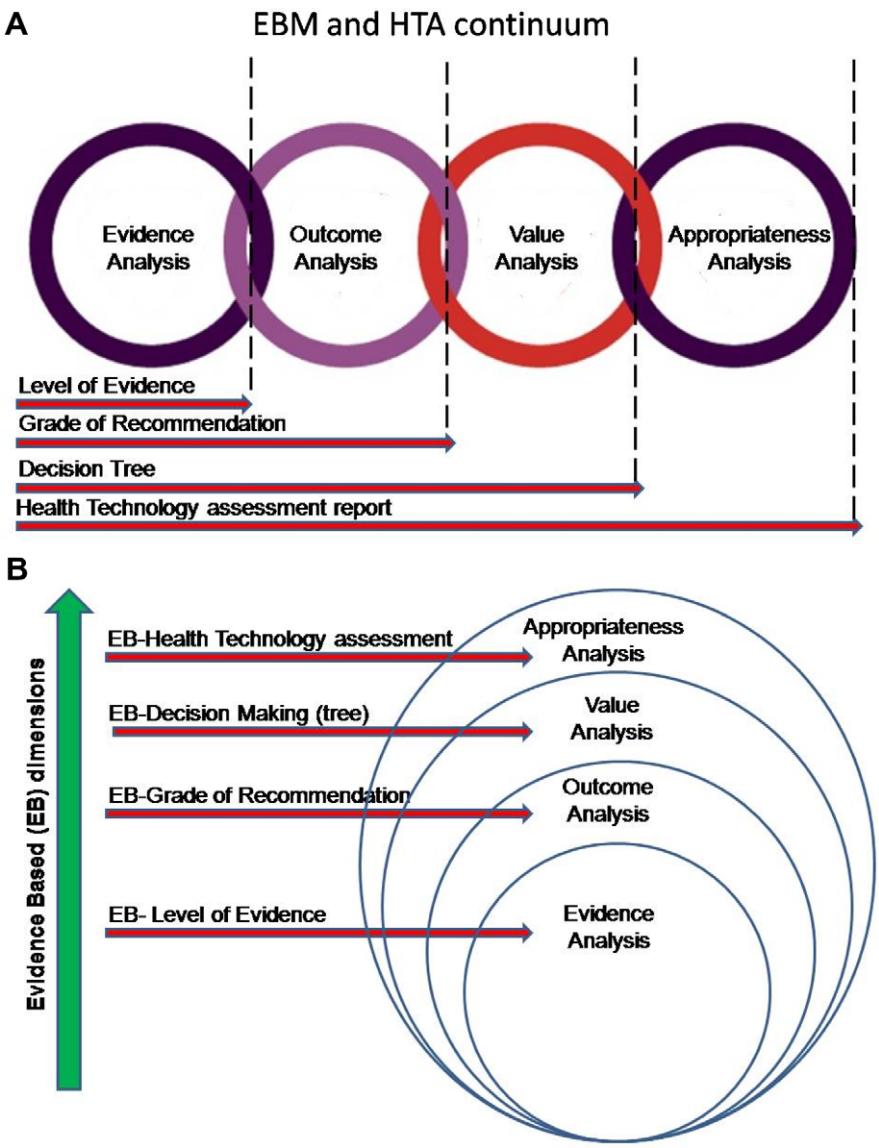

Figure 4 (A) EBM and HTA. (B) EBM and HTA.

(Eddy, 2005). One is evidence-based individual decision-making (EBID). As the name implies this type of EBM focuses on the evidence pertaining to an individual patient's management. As originally proposed, it emphasizes the education of physicians in how to bring evidence to bear on decisions about individual patients (Evidence-Based Medicine Working Group, 1992), and the synthesis of evidence with clinical judgment (Sackett et al., 1996). The other part is evidence-based guidelines (EBGs) and clinical recommendations (CR). This part describes the importance of basing population-based policies like recommendations, guidelines, policies, decisions, and performance measurement on evidence and it is this part that stresses the principle that before any population-based policy can be promoted there should be good evidence about favorable effectiveness and benefit/harm ratio. The next wider scope of this population based or more generally evidence-based practice policymaking will involve more economical and societal factors that influence the whole health system. Thus the continuum of EBM and HTA can be illustrated in Fig. 4A and B which you may call "*EBM–HTA chain*."

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