Investigation of comparative effectiveness research in Asia, Europe, and North America

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ABSTRACT

Comparative effectiveness research (CER) is an important branch of pharmacoeconomics that systematically studies and evaluates the cost-effectiveness of medical interventions. CER plays instrumental roles in guiding government public health policy programs and insurance. Countries throughout the world use different methods of CER to help make medical decisions based on providing optimal therapy at a reduced cost. Expenses to the healthcare system continue to rise, and CER is one-way in which expenses could be curbed in the future by applying cost-effectiveness evidence to clinical decisions. China, India, South Korea, and the United Kingdom are of essential focus because these countries’ economies and health care expenses continue to expand. The structures and use of CER are diverse throughout these countries, and each is of prime importance. By conducting this thorough comparison of CER in different nations, strategies and organizational setups from different countries can be applied to help guide public health and medical decision-making in order to continue to expand the establishment and role of CER programs. The patient-centered medical home has been created to help reduce costs in the primary care sector and to help improve the effectiveness of therapy. Barriers to CER are also important as many stakeholders need to be able to work together to provide the best CER evidence. The advancement of CER in multiple countries throughout the world provides a possible way of reducing costs to the healthcare system in an age of expanding expenses.

KEYWORDS: Comparative effectiveness research, health care costs, pharmacoeconomics

Introduction

The primary objective of comparative effectiveness research (CER) is to improve the national public health and reduce healthcare expenditures by supporting the conduct of research, producing evidence-based guidelines, and implementation of the organization's recommendations.¹² CER programs have a wide range of scope of their research. Drugs, medical devices and procedures, public health interventions and programs may be evaluated.²¹ Overall, most CER organizations assume the payer perspective in economic analysis and hence are mostly concerned with health care costs. Depending on the program, the cost is not always explicitly included as a factor in decision-making. CER programs generate standardized treatment guidelines based on large clinical trials and other high quality evidence trials. CER programs principally based their decision-making on high-quality clinical evidence provided by systematic reviews and meta-analysis when formulating coverage and policy decisions. In turn, research promoted by CER organizations must be translated into beneficial social health policies and procedures that inform clinical decision-making and

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optimize health outcomes. To accomplish these medical goals, CER organizations must disseminate treatment guidelines and policy recommendations and update healthcare professionals. However, evaluation of the extent of CER organizations’ impact on medical decision-making and reception by local and regional organizations is difficult to conduct.

The Institute of Medicine, an International Organization Committed to promoting safe and effective medical care, provides detailed guidelines of what national CER programs must address and procedures they must follow in order to be sustainable and effective. First, CER studies need to be based on public health needs and have adequate financial and technical resources to conduct research. Rigorous methodology must be applied when evaluating studies and determining their scientific merit and public health utility. For studies conducted by the CER organization, centralized data networks should be established for data collection. Stakeholders, including medical professionals and patients, need to contribute to CER programs at all stages of developing guidelines. Supervision by governmental advisory panels is advised to promote efficiency and quality of CER programs. Finally, CER programs should periodically provide reports to the government of improvements in healthcare resulting from CER.

Between nations, CER programs greatly vary with respect to their relationship with the nation’s government. Some CER programs are governmental agencies, whereas other CER bodies are private entities. The role of the government has implications for how much influence CER has on public health policies. In socialized nations, the government pays for a substantial portion of medical care, which means that CER can inform decisions on which drugs and devices the government will insure based on data regarding safety and effectiveness. Ultimately, this means that CER affects which drugs are listed on the formularies of nations and hence are completely reimbursed by the government.

As health care costs continue to escalate, attention to the importance of CER grows. The recent expansion of CER programs in the United States provides insight into recognition by the government of the cost saving utility of CER organizations. According to the Centers for Medicare and Medicaid Services, the United States healthcare expenditure was $253 billion in 1980 but rapidly grew to about more than $2.3 trillion in 2008, accounting for 16.2% of the nation’s Gross Domestic Product (GDP). In 2008, the United States had the highest per capita healthcare expenditure compared to other developed countries, reaching $7124. In 2005, health research spending in the United States totaled $111 billion with approximately $35 billion spent by the pharmaceutical industry, $16 billion spent by biotechnology industry and $10 billion spent by medical technology industry. However, most of this research focused on advancing new technologies and drugs instead of analyzing their cost-effectiveness. The Patient Protection and Affordable Care Act was enacted by the United States President Barack Obama in 2010 to reduce the growth of national health costs. Under this legislation, health insurers were forced to expand insurance coverage by eliminating annual caps and lifetime coverage screenings and immunizations, and preventing exclusions from the preventive care. Thus, in 2009, to ensure health care quality while controlling costs, the US allotted about $1.1 billion to accelerate CER under the American Recovery and Reinvestment Act.

CER conducted in industrialized nations provides developing countries with the necessary guidance for establishing and managing an efficient and sustainable comparative effectiveness program in lower resourced areas. This article describes core features of CER in the developed world and takes a look at low to middle-income countries with a strong potential for conducting CER by building upon the experiences of the developed world. First, we assess the current healthcare and government environment of countries. Next, we closely investigate the state and potential of CER programs to reduce healthcare expenditures and improve healthcare outcomes in these countries. To illustrate the potential of comparative effectiveness evaluations globally, we consider the example of two developing economic superpowers in Asia, India, and South Korea, which illustrate some of the potential advantages and hurdles of developing comparative effectiveness evaluation systems.

India

The Pharmaceutical Industry in India

Pharmaceutical companies in developed nations have been seeking to expand into developing countries with emerging economies. With the growth of pharmaceutical companies, CER can give guidance on which therapies are the most cost-effective. India’s sustained economic development, health care reforms, and patent-driven legislation are helping to fuel the advancement of the Indian pharmaceutical market. Increasing demand for medical treatments for chronic disease conditions coupled with the expansion of medical infrastructure and health insurance provides opportunities for pharmaceutical companies to grow. Moreover, the economic environment of India facilitates pharmaceutical companies’ opportunities including: The doubling of disposable incomes, two-fold increases in the number of middle-class households, and the adoption of product patents and increased market share owned by smaller pharmaceutical companies. In 2005, the Indian pharmaceutical industry was estimated to be worth $6.3 billion with an annual growth rate of 9%. In 2013, it is projected that the Indian pharmaceutical industry will reach $20 billion with an annual growth rate of 12.3% and will increase from the 14th to one of the top 10 positions in the world. The Indian pharmaceutical market’s growth has been estimated at $14 billion in 2013–2014 and is considered the third largest booming market in the world.

Role of the Indian Government

Even though universal health insurance has not been implemented in India, about 19 million people in India are currently covered under Rashtriya Swasthya Bima Yojana, a health insurance provided by the central government for mostly covering people below the poverty line. By 2020, India plans to increase its annual healthcare expenditure from 1.6% to about 3% of the total GDP by increasing access to care and upgrading infrastructure in primary and secondary healthcare centers, such as district civil hospitals and community health centers. Government reimbursement of pharmaceutical products is expected to increase from $1 billion to $4.5 to $6 billion.
by 2020, depending upon the extent of the pharmaceutical industry’s development. Of these pharmaceutical products reimbursed by the Indian government, 45% is allocated to hospitals run by the state and 30% to hospitals managed by the central government. These hospitals can play a vital role in influencing researchers and policy makers by providing a suitable environment for CER through designing treatment protocols and by providing quality of care comparable to the private hospitals.

The Central Drugs Standard Control Organization is the national government agency in India which focuses on the quality of drugs and medical devices in India. Maharashatra, a state in Western India, has its own Food and Drug Administration (FDA) Maharashatra. Adoption of CER at a national level in India can be done by initiating evidence-based planning and management and building a capacity for effectiveness analysis. The evidence-based planning and management for the CER involves framing decisions about the technical and financial management of CER on the basis of the available comparative information about the costs and benefits of health services. For this purpose, it is necessary to develop efficient databases providing information about the financing, expenditures and CER related to health services. Building a strong capacity for performing effectiveness analysis will help in decision-making related to the usage of the most appropriate and cost-effective health technology. In order to build a strong foundation for CER and promote rational use of healthcare interventions, it is necessary to involve different healthcare providers to disseminate evidence about the safety and effectiveness of available treatments to their patients.

South Korea

Healthcare System in South Korea

In South Korea, implementation of universal health coverage has led to the advent and expansion of CER. Universal coverage was first pursued in 1977 and fully implemented in 1989 by the National Health Insurance (NHI) system. As a result of the universal coverage, health care costs have drastically increased. In a period of just 5 years, the annual deficit experienced by the NHI in 1997 developed into cumulative deficit in 2001. The financial crisis in the health sector has brought about urgency among South Korean government health agencies to continuously supervise constantly increasing drug expenditures and diligently pursue the usage of economic data in pharmaceutical reimbursement decisions. In order to optimally use economic data related to drug pricing and reimbursement, the Health Insurance Review and Assessment Service put together the Guidelines for Economic Evaluation of Pharmaceuticals in South Korea in 2005. These guidelines were drawn collectively on the basis of expert reviews, public hearings, and a parliamentary discussion session held in the first half of 2006 and instructed pharmaceutical companies about the preparation of economic data prior to submission of a drug for reimbursement and pricing approval.

In May 2006, the positive list system (PLS) was created as a component of the Health Insurance Review Agency to systematically evaluate economic data for drug reimbursement decisions. In the PLS system, drugs are eligible for reimbursement only if they have data clinical data demonstrating efficacy and cost-effectiveness. Conditional coverage was made available for orphan drugs and oncology drugs which may not have strong evidence of cost-effectiveness. In 2007, value-based pricing was included in the PLS, thereby making the PLS an integral part the Korean health system. The Korean parliament enacted a law in 2008 to provide infrastructure for building research capacity and supporting initiatives undertaken by Health Insurance Review and Assessment Service. This law led to the foundation of the National Medical Research Institute. The research conducted by Health Insurance Review and Assessment Service mostly focuses on head-to-head trials, quality-adjusted life year studies, administrative data analysis, and studies relevant to Korean social value system.

Impact on Pharmaceutical Industry and Rational Use of Pharmaceuticals

Initiation of the PLS helped to rectify the serious shortcomings of the drug reimbursement system under the NHI. Under the NHI, expedited inclusion of new medications approved by the South Korea FDA made many medications eligible for government reimbursement. Consequently, irrespective of cost-effectiveness and budgetary concerns, the NHI drug formulary included 21,000 medications eligible for reimbursement. In contrast, most of the Organization for Economic Co-operation and Development whose goal is to promote economic solutions through the united development of strategies by its members, do not have more than 5000–8000 medications on their drug formularies. The NHI also had major impacts on the pharmaceutical industry. The numerous drugs on the formulary list of NHI attracted competition among many regional Korean pharmaceutical companies. These companies resorted to many illicit and unjust sales promotion techniques to boost their market share values. Most significantly, drug prices continued to increase under the NHI.

Due to the introduction of new pharmaceutical products in the Korean market at an alarming rate, South Korea was among the few countries in the world with the highest number of drug reviews from 2003 to 2005. The South Korea FDA reviewed as many as 25 new medications out of 61 in 2003. The accelerated review of drugs under the NHI motivated pharmaceutical industries to seek approval in South Korea instead of other countries. In conclusion, the NHI reimbursement system lacked optimal drug pricing and requirements for cost-effectiveness data for the newly approved medications. According to the World Health Organization, in the wake of adequate resource constraints, it became necessary for South Korea to regulate the introduction, usage, and reimbursement of medications rationally. Since enactment of the PLS in 2008 by the South Korean government, the PLS provides rational, value-added and cost-effective healthcare resources and services by employing a value-based pricing strategy contingent on clinical and cost-effectiveness evidence. A study of 91 reimbursements conducted over a 2 years period using PLS showed that the recommended decisions were competent decisions and were warranted.

A CER program, the National Medical Research Institute, was formally established in February 2008. The CER agency’s areas of focus include evaluation of clinical trials, analysis

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of claims data, pharmacoeconomics research, and research methodology. This research agency seeks input from the Korean population on social value.

**China**

**Healthcare System in China**

In China, the medical insurance system is not centralized and instead is primarily controlled by local governments. In large cities like Shanghai, the local government collects about 8.5% of employees’ monthly salary as premiums, with employers contributing 7.5%. Comprehensive medical insurance sets up deductable amounts or percentages for each service covered, depending on whether these charges or expenses occur in primary, secondary, or tertiary hospitals, and the insurance usually pays a maximum of 95% of the total charges. Unemployed citizens buy their own medical insurance from either the local government or private insurers. Disabled individuals pay 200 Yuan as a yearly premium to cover 50% of emergency related charges and 30% of inpatient charges.

In recent years, health care expenditures have been rising in China, a phenomenon similar to that occurring in other countries. According to China’s National Health Survey in 1998 and 2003, rural residents’ health expenditures grew at an annual rate of 11.48%, 4 times faster than their net income over the same period. In this setting of disparity between income and health care expenditures, families may have to borrow money or sell assets to pay for health expenses for their sick family members. The distribution of payment for health care in China is also uneven between rural and urban populations, leading to inequality in coverage.

**Technological Infrastructure in China**

In China, CER helps to slow down rising healthcare expenditures due to sophisticated and expensive technologies mostly imported from the Western hemisphere. For example, one study showed that in 2007, China imported costly medical technology including 80% of the computed tomography scanners and advanced medical monitoring systems, 85% of the medical laboratory instruments and 90% of ultrasonic devices, magnetic resonance equipment, and electrocardiograph machines. China imports $24 billion worth of the drugs lamivudine, peginterferon, and imatinib annually for treating hepatitis B, hepatitis C, and chronic myeloid leukemia alone. Besides expensive drugs, overuse of highly technical tests and equipment also contributes significantly to high healthcare expenditures. Since 2005, the healthcare system has been partially privatized. Hospitals no longer obtain fixed reimbursements from the government for performing services. Consequently, there has been an increasing trend in offering more expensive tests and imported drugs, which clearly contributes to the hospitals’ profits, which in also results in incentives for the doctors’ incomes.

Multiple examples of this interplay between efficacy and personal or corporate wealth exist for many common conditions. For instance, physicians may prescribe an imported drug that costs 250 Yuan for imported drugs instead of domestic medicine that only costs 40 Yuan per week and is equally effective and safe.

However, CER provides insight about existing and novel treatment interventions and strategies for selecting the least expensive and most effective medical procedures and therapies. It is possible that some health care professionals who stand to gain more personally from utilization of higher cost drugs may be deterred from encouraging these, if a CER study shows that higher cost drugs are not as cost-effective as the lower cost alternatives. Collectively, a body of rigorous CER may lower health care costs substantially.

The National Institute for Clinical Excellence and Comparative Effectiveness Research in Asian Countries

The National Institute for Clinical Excellence (NICE), reaches out to other countries to help them build their own CER programs in their nations. International delegates of NICE travel to countries and meet with public health officials at workshops about developing guidelines and managing CER programs. NICE provides technical assistance and advice on operating CER programs to India and China. Additionally, NICE aids developing countries in Asia including Vietnam and Thailand.

NICE is an established CER program in the United Kingdom, but it does not receive financial assistance from the government for its recommendations. NICE is a division of the United Kingdom National Health Service, which is the public health regulatory agency. Public involvement in the processes of developing NICE guidelines is greatly encouraged, including on enforcement of guidelines. NICE is enacted differently in various regions of the United Kingdom. First, public local primary care and hospitals have to note a need for resources to institute national guidelines. However, there are significant financial barriers to implementing guidelines due to lack of mandated NICE recommendations. The Care Quality Commission, formerly known as the Healthcare Commission, is a government agency responsible for monitoring and rating healthcare providers’ adherence to mandated NICE guidelines. Introduction of the Care Quality Commission in 2010 now requires providers to meet NICE standards for assessments of technology and performance of medical procedures in order to register as providers.

Figure 1 represents a protocol for writing a comparative effectiveness review.

Table 1 summarizes the parties in nations who met with NICE and the purposes of the meetings during their diplomatic visits to countries.

Some Unique Aspects of Methods to Inform Decisions in Other Countries

While most countries use some variation of topic selection, assessment and appraisal, and consideration of costs as implemented by NICE, some countries demonstrate unique approaches.

Internationally, CER regulatory agencies vary with regard to their methods utilized in topic selection, assessment and appraisal, and consideration of costs. Although most countries generally follow NICE’s model, some countries have unique aspects of their CER programs. Table 2 provides a comprehensive summary comparing the CER regulatory agencies in countries employing unique approaches to the steps
Figure 1: Protocol for writing a comparative effectiveness review[24]

**Development of a Comparative Effectiveness Review:**
1. Use of a patient centered approach
2. Full understanding of the rationale guiding the delivery of specific healthcare service
3. Collection of evidence by prioritizing quality and effectiveness of the service delivered
4. Presentation of pros and cons of the different services available in a consistent manner for fair assessment
5. Use of best practices when empirical data is insufficient or missing

**Selection of topics for conducting Comparative Effectiveness Review:**
1. Application of consistent criteria for selection of potential topics
2. Clearly define the rationale for topic selection
3. Maintenance of transparency and accountability

**Resources for collection of evidence to compare treatment interventions or therapeutic agents or medical devices:**
1. Help can be sought from the experts in the field or administrative staff like librarians
2. Published data, grey literature like unpublished manuscripts, abstracts, clinical registry data, regulatory data
3. Unpublished data from pharmaceutical industries
4. Use of multiple databases
5. Well documented and completely reported data

**Assessing the risk of bias for selected studies in comparative effectiveness reviews for comparing treatment interventions or medical devices or therapeutic agents:**
- Risk of bias should be assessed based on:
  a. Appropriate sensitivity analyses and defined decision rules
  b. Selection, selective outcome reporting, attrition, performance and detection
  c. Use of valid and reliable tools as measures of detection bias and performance bias respectively

**Assessment of harms of comparing treatment interventions or therapeutic agents or medical devices:**
1. Experts in the field should play a key role in identification of harms
2. Use of consistent terminology for reporting harms
3. Appropriate use of methods for assessing benefits does not guarantee the same for harms
4. Use of multiple sources for collection of evidence on harms when generalizability is an issue
5. Caution should be employed for combining evidence on harms
6. Placebo-controlled trials can be handy for assessing rare or harms

**Performing the quantitative analysis for comparing treatment interventions or therapeutic agents or medical devices:**
- Based on the data available the following can be employed:
  1. Meta-analysis
  2. Indirect comparison
  3. Effect measures like relative risk, odds ratio, rate ratio, mean differences, Hedge’s g, Cohen’s d or Glass’s
  4. Different models like a random effects model, a fixed effects model, the Peto OR method, the Mantel-Haenszel method, Bayesian methods, fixed effects logistic regression
  5. Testing the model for heterogeneity
  6. Combining different study designs like cross-over trials, cluster-randomization trials, Clinical trials, observational studies
  7. Performing Sensitivity analyses to determine the robustness of the combined estimates and assumptions made in the review

**Assessing the validity of the evidence collected for comparing treatment interventions or therapeutic agents or medical devices:**
1. Testing risk of bias, precision, confounders, dose-response relation, publication bias, degree of association, consistency of results and directness.
2. The evidence might be graded on the basis of varying degrees of strength: High, medium, low, inadequate
3. Evidence associated with each major outcome should be graded separately

**Using existent systematic reviews for replacing de novo processes for writing a comparative effectiveness review:**
1. A part of or complete DeNovo process can be replaced using existent systematic reviews of high quality
2. Achievement of agreement between the CER and existent systematic reviews is necessary
3. Existent systematic high quality reviews can be used in the CER using:
   a. Summarized evidence from existent systematic reviews
   b. Replacing the key question of the DeNovo process using a single existent systematic review or a combination of many existent systematic reviews
4. Reference lists of the existent systematic reviews should be reviewed on a regular basis
5. Comparison of the results of the DeNovo process and the existent systematic reviews for achieving consistency
Table 1:

| Country | Year of meeting | Location and purpose of meeting |
|---------|----------------|---------------------------------|
| India   | October 2009   | Hyderabad                      |
|         |                | Agencies involved: Indian Institute of Public Health, Ministry of Health and Family Welfare |
|         |                | Purpose: Methods for developing guidelines and setting health priorities, applying NICE techniques to health care region |
|         |                | Kerala                         |
|         |                | Agencies involved: Ministry of Health of Kerala, Clinical Epidemiology Resource and Training Centre |
|         |                | Purpose: Gain understanding of guideline development methods and provide input on Rural Health Mission Reforms, provide technical and operational support |
| China   | October 2009   | Rural China                    |
|         | July 2010      |                                |
|         |                | Agencies involved: China National Health Development and Research Centre (CER agency) |
|         |                | Purpose: Assessment of Clinical Pathways project (part of legislative Rural Health Reform initiative) and surveying stakeholders on this project; provide training on conducting cost analysis |
|         |                | Beijing                        |
|         |                | Agencies involved: Ministry of Health and Ministry of Human Resources and Social Security |
|         |                | Purpose: Discuss methods of evaluating hospitals and providing academic incentives |
| Thailand| March 2009     | Bangkok                        |
|         |                | Agencies involved: Health Technology Assessment Agency of Thailand |
|         |                | Purpose: Evaluated the CER organization’s performance and its publications |
| Vietnam | January 2011   | Hanoi                          |
|         |                | Agencies involved: World Bank and the Oxford Clinical Trials Unit, Ministry of Health, Department of Planning and Finance, Department of Health |
|         |                | Purpose: Provide input on Vietnam’s efforts of implementing health reforms, introduce NICE’s work and role in international affairs, form coalition in supporting health care reforms |

NICEs=National Institute for Clinical Excellences, CER=Comparative Effectiveness Research

Table 2:

| Country (CER agency); date founded | Key characteristics |
|-----------------------------------|---------------------|
| Germany (Institute for Quality and Efficiency in Healthcare); 2004 | Structure: Board of Trustees, Scientific Advisory Board, Steering Committee, Methods Group independent of government |
|                                   | Research focus: Drugs, devices, and medical procedures |
|                                   | Type of evidence: Meta-analyses of randomized controlled trials |
|                                   | Other: Authority to issue recommendations on maximum insurance reimbursement for medical technology |
| Australia (Pharmaceutical Benefits Advisory Committee); 1953 | Structure: Four academic evaluation groups and speciality economics and drug utilization subcommittees |
|                                   | Research focus: Evaluation of prices submitted by pharmaceutical companies on the basis of clinical analysis and conducts negotiations according to cost-effectiveness |
|                                   | Type of evidence: Manufacturer data, cost-effectiveness analysis |
|                                   | Other: Greatly influences listing of drugs on the national formulary, but subject to approval by Minister of Health and Aging |
| Canada (Ontario) (Ontario Health Technology Advisory Committee); 2003 | Structure: Ontario Medical Association and the Ontario Hospital Association |
|                                   | Research focus: Medical devices and technologies |
|                                   | Type of evidence: Field evaluations include randomized controlled trials and establishment of registries |
|                                   | Other: Initiates its own studies, called conditionally funded field evaluations, if assessing evidence that is not strong enough to inform medical decision-making |
|                                   | Ontario’s Institute for Clinical Evaluative Sciences |
|                                   | Structure: Directly connected to government |
|                                   | Research focus: Training researchers in assessing health care services and clinical epidemiology |
|                                   | Type of evidence: Claims and administrative data |

Contd...
in CER development. In particular, we highlight the similarities and differences between the structure, areas of research focus and types of evidence utilized in policy decisions. These specific agencies assist in the decision-making and policy formulations of CER programs in other nations. [25]

**Discussion**

CER is an important concept in healthcare to help curb costs while still maximizing the quality of patient care. The patient-centered medical home (PCMH) is an innovative concept that tries to improve the quality of healthcare while striking a balance with the costs associated with healthcare. The Affordable Care Act established PCMH in the United States. [26] The PCMH is focused on improving quality, cost, and overall experience of the primary care. [27] There are several key components of the PCMH that are used to help improve the quality and cost of healthcare. [17] The first component is that each individual patient is given one primary care physician who oversees all of the healthcare needs of the patient, which includes both acute and nonacute situations. Another key component of the PCMH is that care is administered by multiple specialists who are under the direction of the primary physician usually via electronic communication. Quality in the PCMH is paramount, and as such physicians are monitored using performance measures to ensure patients are getting better and that outcomes are being met. A fourth component of PCMH is an increased access to care, which includes more access to physicians and health care systems. This could be through an increased amount of personalized communication or more hours of operation being enacted. The final component is how costs are associated with the PCMH. Under the PCMH, the physicians are reimbursed more appropriately for providing better outcomes for patients. For example, if patients are receiving better care, than a decrease in hospitalizations will be seen, which ultimately saves the health care system money through cost savings. Enhanced reimbursement for communication and incorporation of health information technology in unison with current CER guidelines would allow for patients to receive better care while curbing costs throughout the health system. [17]

CER is critical to apply to the PCMH because it will reduce costs further by using guidelines that provide an increased cost savings. CER will provide evidence on which medications will provide the greatest efficacy for the lowest cost. This will allow physicians to incorporate these CER guidelines in their practice to provide patients with equivalent outcomes for a reduced cost burden. A study in the American Journal of Managed Care showed a 7.1% total cost savings using the PCMH model over a 3 year time period. [25] The study also showed that increased preventative tactics reduce the costs in the future by preventing worsening of chronic conditions. [27] This CER is vital to help incorporate PCMH and other models into the healthcare system because evidence is needed before models can be justified and cost savings can be realized. According to the Centers for Disease Control, 13 CER studies have reported a cost savings when using the PCMH and studies have also shown a more beneficial patient experience. [28]

CER is important to many developing countries, as well as more developed countries. In the future, CER will be vital to help reduce costs with the escalating expenses of health care globally. Establishing guidelines that both improve patient care and reduce costs is the primary focus of CER. The increased cost burden has been felt on a global scale and CER is developing as a way to contain some of those costs. Most countries have set up a board or agency to help establish evidence and guidelines based on CER to provide patients with better outcomes while not incurring too much of a cost burden.

Further studies need to be conducted to determine, what the best form of structure, focus, and evidence is used when evaluating healthcare outcomes and costs. Globally many countries use some form of CER to evaluate health care costs and outcomes, but none of the structures has been proven to be the best structure.

Adoption of CER has some barriers that must be overcome so that cost savings can be realized. [22] All stakeholders including patients, physicians, and government agencies must work together; or CER will not be able to be implanted successfully. [22] Experts in pharmacoeconomics are needed to interpret CER to be able to translate results from studies into the health care system. [12] The establishment of a centralized data forum must be completed to ensure that information is available on a global scale and that countries from around the world have access to CER. [16] CER also must be adopted by the health care

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**Table 2:**

| Country (CER agency); date founded | Key characteristics |
|-----------------------------------|---------------------|
| France (High Health Authority); 2004 | Structure: Independent public body with a body and a specialist committee Research focus: Drugs and devices Type of evidence: Prices medical technology using a five-point scale based on degree of medical improvement Other: Legally mandated to include cost in evaluations, but only actually considers cost in the case of class comparisons |
| Sweden (Pharmaceutical Benefits Board); 2002 | Structure: Creates positive drug list of medications eligible for government reimbursement Research focus: Drugs Type of evidence: Comparative clinical and cost-effectiveness analysis, clinical data, and economic evaluation Other: Assumes societal perspective in pharmacoeconomics evaluations |

CER=Comparative Effectiveness Research
system, which over the past decade has proven problematic. Decision makers must be careful to avoid using confirmation bias, pro-intervention bias, and pro-technology bias when evaluating CER and applying it to practice. CER also must report on the information that payers, providers, and patients need and not superficial information that does not help to make clinical decisions. The limited use of clinical support technology has also hurt the widespread use of CER because clinical support technology helps clinicians become more familiar with guidelines and also improves physicians’ ability to analyze data. A standardized format of conducting CER would be beneficial to provide a better global use of CER.

**Conclusion**

CER has the potential to provide many opportunities for countries across the globe to reduce their cost burden and maintain the optimal outcomes for patients. Many countries have begun to take steps to start using CER in their evaluations of which medications or medical devices are reimbursed. The PCMH model is an application of how CER can be used to help curb costs while still maintaining optimal outcomes. The enhancement of information technology will help to provide a database for CER to allow countries across the globe to evaluate CER to best determine economic decisions in their country. It is imperative that evidence-based research is used to help curb costs in developing countries to help prevent escalating health care costs. As CERS programs continue to develop in countries around the world, evidence will be used to help inform decision makers to provide the most cost-effective solutions while still maintaining the efficacy of treatments.

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**Conflicts of Interest**

There are no conflicts of interest.

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