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Review

Applying evidence to patient care: From population health to individual patient values

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ABSTRACT

What are the health status and health needs of people with epilepsy? How do clinicians and patients choose between alternative interventions for the same condition? Are health interventions used effectively in the community, and do they improve health? How can we translate findings from regulatory clinical trials to the real world? These and similar questions are the subject of applied translational research. This evolving and broad-ranging area of research involves the application of basic sciences such as epidemiology, biostatistics, economics, and behavioral science to the assessment of health, health interventions, and outcomes. However, despite its palpable importance, applied translational research remains underfunded and underutilized. Using their own innovative research as a prototype, two young and promising investigators provide insights not only into the enormous potential but also the gaps and hurdles of two specific areas of applied translational research, i.e., clinical decision analysis and health services research. The message is clear that if we are to understand and improve the health of people with epilepsy in clinics, hospitals, and communities, we must substantially increase research capacity to address the many gaps that thwart our progress in applied research in epilepsy.

This article is part of a Special Issue entitled "The Future of Translational Epilepsy Research".

1. Introduction

Translational research is conceptually and operationally divided into two stages. The first stage involves translating findings from bench to bedside, from basic discovery to application in humans. The second stage involves translating knowledge from clinical trials to actual patient care and to the health care of populations. For researchers focusing primarily on health care and health outcomes, translational research is all about the second stage, ensuring that new treatments and research knowledge reach the patients and populations for whom they are intended and that they are implemented correctly. The discovery and clinical testing of new treatments and diagnostic markers in the laboratory (first stage translational research) are but the starting point for the translational researchers who seek to improve health and quality of care by improving access and systems of care, by helping change behaviors and clinical culture that lead to better informed choices, and by providing relevant clinical decision support tools. Nonetheless, the overwhelming emphasis of researchers, academic centers, and funding agencies has been on the first stage of translation. The US invests about 4.5% of its total health expenditures on biomedical research, but only 0.1% supports research in health services, comparative effectiveness, new care models, quality, outcomes, and service innovations [1].

2. What does it take to translate clinical research to patient care?

Why is it that patients in the US receive only 55% of recommended care? Additionally, why is the rate lowest for complex interventions such as for alcohol dependence (11%) and highest for simple surgical interventions such as cataract surgery (79%) [2]? The American Academy of Neurology systematically identified 160 published care recommendation statements which were distilled into eight indicators of quality of care in epilepsy. These include documentation of seizure type, frequency, injuries, medication side effects, EEG and MRI results, and dates performed, whether the patient has well-controlled or intractable seizures at every visit and consideration for surgical referral if refractory [3]. However, it remains unknown to what degree these are being applied to patient care and how impactful they are. There is disconcerting evidence that evidence-based practice guidelines for surgical and medical care in epilepsy have not made a discernible impact on clinical care [4–6]. The reasons are manifold and complex, illustrating the urgent need for more extensive research into applied knowledge translation.

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As eloquently stated by Woolf, "Successful health interventions in hospitals, homes, and communities require the translation of other "basic sciences" – such as epidemiology, behavioral science, psychology, communication, cognition, social marketing, economics, political science – not only the translation of biotechnological insights and novel therapies. These disciplines deserve their place not only in definitions of basic science but also in funding priorities. Poverty matters as much as proteomics in understanding disease" [7].

Applying different research methodologies aimed at improving the health care and health status of people with epilepsy, two young epilepsy researchers are making a difference in this "second stage" of translational research. Using clinical decision analysis (CDA) modeling, Dr. Hyunmi Choi illustrates the elegance of a summary outcome metric, the Quality Adjusted Life Expectancy, which explicitly encapsulates an array of probabilities, values, and time courses of patients who undergo surgical or medical therapy for temporal lobe epilepsy (TLE). Dr. Choi's eloquent and highly practical decision analysis for choosing therapies in patients with TLE stands in contrast to the obvious research gap in epilepsy using CDA methods. Despite the broad applicability of CDA at the level of health policy and resource allocation, as well as at the level of clinical management, the dearth of such studies in epilepsy has persisted unchanged for the last 15 years. Possible explanations for these gaps are proposed.

In a short period of time, Dr. Nathalie Jette has become a master in health services research (HSR). Adept at addressing the tough methodological issues required to extract wisdom from large and complex datasets, Dr. Jette uses her own HSR studies to illuminate the unique advantages of HSR, which include the ability to translate evidence from clinical encounters to the health of populations and back to the clinical setting. Dr. Jette demonstrates that research using health surveys and practice-based data has much to contribute to the translational research spectrum, but important gaps need to be addressed. She illustrates some of the work undertaken by her team to close these gaps.

3. Promising areas of research and young investigators

Hyunmi Choi

Gaps in decision analysis and patient valuation of health states

Outcomes research is "a line of health services research that focuses on identifying variations in medical procedures and associated health outcomes" [8]. Among the extensive array of methods and tools used in outcomes research, clinical decision analysis (CDA) provides quantitative analysis of each available medical choice or intervention when making decisions [9]. Clinical decision analysis is particularly helpful in clinical situations in which there is uncertainty about outcomes relating to alternative courses of action, and it can facilitate the decision-making process at a health policy level and at the individual patient level for clinical encounters. When clinical decisions compare interventions in terms of costs and health outcomes, CDA incorporates the cost-effectiveness analytical approach. Thus, CDA serves as a foundation for cost-effectiveness studies, whereby costs of interventions, valuation of costs, and preferences for health outcomes from interventions are integrated to produce costs per unit of outcome for each medical choice [10].

Clinical decision analysis and related methods (e.g., cost-effectiveness analysis) have been highly valuable in many areas of medicine. Influential studies published in preeminent journals have used CDA to determine, for example, whether or not to use anticoagulants to prevent stroke in patients with non-valvular atrial fibrillation [11] or whether or not to perform prophylactic mastectomy in women with *BRCA1* or *BRCA2* mutations [12]. Clinical decision analysis is particularly relevant in epilepsy because large scale randomized controlled trials (RCTs) for relevant interventions are scarce and difficult to conduct. Here, CDA offers a scientifically rigorous alternative to answer clinical research questions.

To gain insight into the application of CDA and related methods in epilepsy, we describe its origins, a framework for conducting CDA using our published work as a case study, and the trends of CDA and related methods in the epilepsy literature in the past 15 years.

3.1. What is CDA?

Derived from game theory, decision analysis was first described by John von Neumann in 1928 [13] and applied to economics in the 1940s [14]. Clinical decision analysis emerged in 1967 when Henschke and Flehinger applied this method in a study to decide whether or not to perform radical neck dissection in a patient with oral cancer without palpable neck metastases [15]. After the early 1970s the number of CDA publications rose, especially in radiology journals, which increased from 1.6 per year during 1985–1995 to 9.4 per year during 1996–2005 [16].

Clinical decision analysis has proved particularly valuable in difficult clinical decisions requiring careful weighting of risks and benefits. For example, among women who carry *BRCA1 or BRCA2* mutations and are at high risk for breast and ovarian cancer, a CDA determined that on average, the life expectancy of 30-year-old women increases from 2.9 to 5.3 years with prophylactic mastectomy and from 0.3 to 1.7 years with prophylactic oophorectomy [12]. For patients facing complex clinical decisions, CDA helps simplify the choice of alternatives.

In addition, CDA can be used on a population level to help set policies and guidelines. A recent CDA helped forecast an increase of approximately 21.3 million cardiovascular events and 7.7 million cardiovascular deaths during 2010 to 2030 in China [17]. Moreover, the analysis estimated that reducing the prevalence rate of smoking to 20% in 2020 and 10% in 2030 in men or reducing mean systolic blood pressure by 3.8 mm Hg would prevent 2.9 to 5.7 million total deaths over 2 decades. Thus, CDA provided a systematic framework that evaluated alternative health reforms and guided adoption of local treatment programs and national tobacco control policies.

Decision analysis can be conceptualized as follows. Once a clinical problem or clinical decision is identified, a decision tree is created to represent the clinical problem. Decision alternatives (e.g., treatments being compared) are identified, and all possible, mutually exclusive, clinical outcomes associated with each alternative are listed as tree branches, representing the possible sequence of events. The probabilities of occurrence of various outcomes are estimated from pooled estimates derived from the best available evidence obtained through systematic review and critical appraisal of the literature and assigning estimates to these chance events. Uncertainty of probabilities is assessed through sensitivity analysis. The relative desirability of living in various health states or outcomes states, called utility or preference-based health-related quality of life, is evaluated from patients or from the general population. Afterwards, the decision tree is analyzed to evaluate the expected benefit associated with each strategy in terms of life expectancy and quality-adjusted life expectancy (QALE). Sensitivity analyses are performed to test whether the results of the baseline analysis remain unchanged when the analysis is re-run with different probability values [18]. Because CDA allows quantification of human preferences, assumptions, and uncertainties in a model, some regard it as a better method of reaching decisions regarding evidence-based practice than meta-analysis, which is limited to summarizing the evidence [19].

A vital challenge in CDA is the accurate quantification of utilities or "values" of each health outcome state included in the model. Utility is a measure of health status but is distinct from health-related quality of life (QOL) measured with instruments such as the SF-36 or QOLIE-89. Unlike QOL instruments, which focus on function, activities, or health domains, utility instruments allow individuals to value their desirability or preference for a particular health state, generating a single numerical value between 0 (death) and 1 (perfect health). Utilities