INDUSTRIAL DAWGS
UGA IPHO NEWSLETTER

VOL. 1, ISSUE 1 MAY 2023

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In This Issue

11/8/2022 - Guest Speaker Event with Dr. Catherine Ross, Dr. Leslie Jaggers, & Dr. Allison Musick Leiger

PROFESSIONAL & SOCIAL EVENTS

Athens Skate Inn Social

IPhO & AMCP Internship Panel

Pharmtoberfest Poster

Trivia Night Social

More Ways To Get Involved

This year included our first regularly scheduled social events as an organization. Attendance at these events was even better than we had hoped, and we thank all of our members who participated. We were well represented at Pharmtoberfest this year by the newly formed committee. Thanks to all of our volunteers who participated on this committee.

Our internship panel held in collaboration with AMCP saw great attendance. We were very glad to have this opportunity allowing some of our more experienced members speak on their recent internships. In the future we hope to continue holding events like these as well as creating more opportunities for everyone to get involved in IPhO.

- Andrew Bennett, Editor

VIP CASE COMPETITON

Competition Team

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This was the first year our IPhO chapter created a team to compete in the national VIP Case Competition. Five months and many meetings later our team created a wonderful presentation that we are very proud of. This experience was a great way to learn more about pharmacist roles in industry as well as a chance to build teamwork skills and meet with industry professionals in various functional areas.

We were also able to create an elective course for our members who participated in the competition. This course was taught by our wonderful advisor Dr. Rekhi, and was a great chance to reflect on all of the information and experiences learned during the competition. We hope to continue joining the competition each year and look forward to seeing how future teams are able to perform.

Patient and Caregiver Experiences with and Perceptions of Risk Evaluation and Mitigation Strategy Programs With Elements to Assure Safe Use

Summary By: Kayla Ward, MBA, Pharm.D. Candidate

In 2007, Congress passed the US Food and Drug Administration (FDA) Amendments Act which allowed the FDA to improve prescription drug safety for specific drugs that have clinically important adverse events. This is currently being put into practice through initiating Risk Evaluation and Mitigation Strategy (REMS) programs with Elements to Assure Safe Use (ETASU) for specific medications to ensure that the benefit of these drugs is outweighing their risks of adverse events associated with them. There is data on how effective these REMS programs with ETASU in preventing adverse events of drugs, however, there is a lack of data involving the experience of patients and their caregivers with REMS programs with ETASU. The objective of this article was to focus on this experience and discover common themes to improve the program in the future.

This qualitative study was approved by the Institutional Review Board at Brigham and Women's Hospital. The specific guideline followed was the Consolidated Criteria for Reporting Qualitative Research (COREQ). Forty REMS programs with ETASU were ranked based on the following criteria: prescriber certification, screening/follow-up monitoring, dispensing restrictions, and manufacture access to patient health information. Out of these 40 programs, four were selected to study for the following drugs: natalizumab, riociguat, sodium oxybate, and vigabatrin. All interviews were held between 2016 and 2017 and the information collected was categorized to be able to distinguish common patterns between interviewees' answers. There was a total of 63 participants; 40% had taken natalizumab, 15% riociguat, 24% sodium oxybate, and 16% vigabatrin. Four common themes were identified: awareness of the REMS program and drug risk, impact of the REMS program on decision-making, access to the REMS-covered drug, and perceptions of REMS-based data collection.

When analyzing the responses to patients' and caregivers' awareness of the REMS program and drug risk, 32% of participants thought that the REMS program was intended to benefit the drug manufacturer or physician and not the patient. 17% of participants thought the forms required for the REMS program were "verbose, overwhelming, and vague." There were multiple suggestions to shorten and simplify these forms in lay terms to make them more user friendly while clearly identifying how patients benefit from these programs. The correlation between the REMS program and decision-making by the patient or caregiver were analyzed next. Of those interviewed, 86% discussed that their decision in taking the drug with a REMS program either had no effect on their decision or it made them more comfortable in their decision to take the medication. Those that stated the REMS program had no effect on their decision said it was primarily due to having previous knowledge from their provider about adverse events or agreed to take the drug before seeing the enrollment forms. REMS with ETASU typically involves a medication guide and communication plan between the patient and the prescriber, but it also may entail patients to receive regular lab work (i.e. blood panel, liver panel, pregnancy tests). Twenty four percent of participants "found the REMS program requirements excessive." Another theme was that 54% of participants felt that it was a burden to pay for the drugs regardless of insurance coverage. Regarding concern of personal health disclosure, 57% of participants feared inadequate data protection was in place. The lack of transparency between why the specific personal information was needed by the manufacturer created worry in the participants. Counteractively, 25% of participants believed that by their willingness to provide manufactures with health information would allow the manufacturers to help further patients.

Common trends in this study were skepticism, powerlessness, and knowledge deficits. There was a large gap in the knowledge about what information was being used for and why it was necessary. If this gap is filled and patients taking these medications are informed about what REMS programs are and why the FDA has put them in place, the feeling of powerlessness and skepticism can be mitigated. The primary purpose of these REMS programs is to ensure drugs with serious, life threatening side effects have more benefit to patients than risks. Industry pharmacists have the opportunity to play a key role in identifying whether new medications may need REMS programs during the initial stages of the drug approval process. This would be critical in further preventing adverse reactions from specific medications and allow for REMS programs to be initiated earlier. Through informing and educating patients about the REMS programs process, they can feel as if they have gained power to aid in a program that will not only protect themselves but will protect future patients on these medications as well.

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Advancing drug safety science by integrating molecular knowledge with post-marketing adverse event reports: a summary

Summary By: Amber D. Fraley, Pharm.D. Candidate 2024

Numerous drugs have been recalled from the market due to unforeseen complications, often revealed later in phase 4 trials. Soldatos et al. propose the use of molecular data as an early warning system, allowing the FDA to watch for specific side effects and recall medications before they can cause serious harm. The authors argue that statistical analysis and placebo-controlled trials are the industry standard yet critically important data about the mechanism of action (MOA) and pharmacology of these medications are lacking.

Ways to analyze medication safety profiles include but are not limited to adverse event collection from clinical trials, knowledge engineering, and data mining. Among all three mechanisms, the many believe there is a lack of standardization and clarification. The authors propose the use of a molecular analysis of side effects (MASE) model, which they claim offers a standardized model for evaluating medications proactively. MASE is based on what the article call a "systems pharmacology" approach. Systems pharmacology refers to the use of pharmacokinetics, genomics, biochemistry, and pathophysiology predicting how a drug may perform in the real world. In addition to side effect data from published clinical trials, MASE can give clues about which side effects should be monitored closely. Additionally, it appears that MASE can give researchers new hypotheses to guide future research. For example, MASE found that beta antagonists may improve mortality for skin cancer patients. Since MASE is a theoretical database, it is unable to directly test these findings on its own, but it can still provide insight into future research targets. Soldatos et al. claim MASE may be a viable starting point for machine learning algorithms in the future, especially given the FDA's recent funding of artificial intelligence driven medication programs.

There are many possible benefits to using systems pharmacology, but various software programs address issues differently. Some platforms such as FAERS or VAERS look at adverse event data that relies solely on practitioner reporting (e.g., angioedema with lisinopril). As a result, there is a lack of statistical analysis since adverse events are not analyzed further for possible associations. A side effect such as hypotension following an IV infusion of paclitaxel may be related to the drug or related to the drug formulation. Other platforms such as OpenVigil and AEOLUS are public data projects that transform the data and produce possible conclusions. The authors note that open platforms provide connections between data elements but may have unintuitive graphical user interfaces (GUIs). Notably, Soldatos et al. mention that semi-commercial solutions such as Molecular Health's Effect, OFF-X, and FDAble have already begun to incorporate molecular information into their data models. Commercial solutions vary and are not uniform, so standardization remains an issue. Soldatos et al. note current software programs can have trouble differentiating between formulations and indications. Therefore, human intervention and research are still needed to sift through software data and determine if the resulting conclusions are clinically relevant.

Molecular data is important to industry pharmacists and pharmaceutical companies looking to minimize costs and maximize patient safety. As the FDA improves its ability to regulate medications, industry pharmacists must be aware of how medications can fail during post-marketing surveillance. Pharmacists who understand how systems pharmacology is implemented into adverse event software can provide pharmaceutical companies with a competitive advantage. Catching problematic medications earlier is crucial to providing regulatory agencies with important safety data, and ultimately saves pharmaceutical industries millions of dollars on advertising and drug development. More importantly, integrating molecular analysis data into safety analyses improves public health and curtails the sale of potentially deadly medications.

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Febridix and Its Role in Ending Antibiotic Resistance

Summary By: Ryan Sarvestani, Pharm.D. Candidate

Febridix and Its Role in Ending Antibiotic Resistance
Acute respiratory infections are among the most common illnesses physicians diagnose in outpatient clinics. Acute respiratory infections can be either bacterial or viral, but many viral infections are inappropriately treated by antibiotics. About 41% of all antibiotics prescribed are used to treat acute respiratory infections about half of which are medically unnecessary.1 This unnecessary use of antibiotics has led to antibiotic resistance which is defined by the World Health Organization (WHO) "the ability of bacteria to resist the pharmacology of the antibiotic, rendering them ineffective".2 Total antibiotic expenditure equals about $8.8 billion USD, additionally antibiotic resistance is estimated to cost the U.S economy $20-$50 billion USD annually1. The total antibiotic expenditure includes direct cost of initial antibiotic treatment as well as second-line inappropriate antibiotic treatment. Second-line inappropriate antibiotic treatment encompass patients returning for a second round of antibiotics when the first round was ineffective. This includes the cost of patients requiring follow up care from the drugs related adverse reactions that affect a total of 11% of patients taking antibiotics, and the cost of antibiotic resistant infections developing from the incorrectly incorporated antibiotic treatment. It is paramount to appropriately prescribe antibiotics not only for the safety of the patients but to relieve the financial load from the United States economy.

Accurately assessing whether antibiotics are necessary for treatment solely based on a physical assessment is difficult. Physicians often turn to a point of care test to accurately assess the patient and inform the clinician appropriately on the decision of disease therapy. FebriDx, a 10-minute point-of-care test, uses fingerstick blood to determine whether the infection is bacterial or viral. This is done by incorporating C-reactive protein, that is elevated in both viral and bacterial infections, and Myxovirus resistance protein A (MxA) which is elevated only in acute viral infection. In the result window of the diagnostic test, a single black strip indicates a bacterial infection whereas any presence of a red strip indicates a viral infection. In multi-center U.S trials, FebriDx was determined to have a sensitivity of up to 95% to detect a bacterial infection and up to 99% negative predictive value to rule out bacterial infection.1 The main benefit of a point-of-care test is the convenience and rapid result time that undercuts the cost of office-based outpatient visits. At the time of publication FebriDx was valued to cost an average range of $23 USD while office-based outpatient visits are valued at an average of $245 USD.1 Using a presumed average Febridx cost of US$23 the expected national cost of using Febridx as a guide for correct acute respiratory infection treatment totaled $5.74 billion USD. Comparing this to the current total expenditure of antibiotic use, the savings using Febridx totaled to be $2.51 billion USD.1 it is important to note that the benefit of Febridx varied depending on the specific type of acute respiratory infection, whether it is sinusitis, otitis media, pharyngitis, or other.

The economic analysis of point-of-care medical device FebriDx is essential for pharmaceutical industry as it offers a comparison of how much money is spent on antibiotics and the projected expenditure of antibiotic resistance yearly. FebriDx is a novel medical device that has been projected to save the Unites States $2.51 billion USD. Its ease of use, rapid result time, and high accuracy allows it to save the healthcare system time and money as well as assuring patient safety with appropriate disease treatment. Industrial pharmacists are involved in design, research, and development of medicines and medical equipment to ensure safety and quality. Pharmacists are recognized as one of the most accessible health care providers and are familiar with many point-of-care testing devices and how to counsel a patient on its use. Having that background, pharmacists can apply ease of use and efficacy of what they encounter from their patient experience to the industry, overall developing a higher quality product. In this case, the role of the industrial pharmacist is understanding the potential outcome of antibiotic misuse, thereby using that concept to ensure safety and efficacy of the medication used to correctly treat the disease state by implementing a test that will accurately assess the most effective treatment for the patient.

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Essential Tremor

Summary By: Alexander J. Collins, Pharm.D. Candidate

Essential tremor is a disorder most commonly afflicting the elderly population with prevalence beginning at age 40 and increasing considerably with age. So, why is essential tremor a threat? In a nutshell, essential tremor (ET) is a movement disorder. Additionally, it is chronic, progressive, and has no known treatment. Because of this, those studying ET for the Journal of Health Economics and Outcomes Research took time to specifically compare the management of essential tremor with multiple comorbidities, various psychiatric disorders, healthcare resource utilization, and costs. The main reason for this study is to underline the importance of ET treatment and optimization to expand treatment outcomes.

This large cohort study primarily observed adult patients over the span of three years. Inclusion criteria for the study included patients with at least one essential tremor medical claim. However, those diagnosed with either Parkinson's disease or thyroid disorders were excluded as these disease states are independent of an ET diagnosis. Patients selected for this study were at least 22 years old and had made other claims of comorbidities within 6 months, or psychiatric disorder claims within 12 months of the index date. The last thing considered for methods was resource utilization and costs of treatment. Each patient that was considered for this study was further observed for any emergency room admissions and inpatient admissions while factoring in their length of stay. The data was broken down into two categories: means (+/- SD) for continuous variables and frequencies (%) for categorical variables. After all of these things were considered, essential tremor patients were put into three categories based on treatments observed in the study: pharmacological, invasive, or untreated. Demographics, medical claims, and diagnosis were all considered in the observational study.

There was a total of 5,286 eligible patients with essential tremor, of which, 49.1% were female. The average age of the cohort was 72 years old, and 79% of them were over the age of 65. The patients were split into three categories. Of these, 71.3% were given some kind of pharmacological therapy, 26.0% did not have any treatment whatsoever, and the remaining 2.7% had invasive therapy. Analysis of the cohort illustrated the most common comorbidities among essential tremor patients were hypertension, pain, hyperlipidemia, sleep discrepancies, and diabetes. Further, majority of the ET patients had at least three comorbidities at a staggering 79.7%. As for psychiatric disorders, presence tended to vary by treatment/age group. Approximately 45.9% of the eligible patients had psychiatric disorders, of which the most common were anxiety, depression, and substance abuse. Patients older than 65 were more likely to have comorbidities while younger patients were more likely to have psychiatric disorders. Lastly, the average ET patient spent approximately $17, 560 per year. When all of the comorbidities were accounted for, increased risk of ET-related higher healthcare costs were disclosed. Some variables that contribute to this risk are urban/suburban living, higher household income, and older age.

This study was the first of its kind—a large-scale, population-based U.S. survey of U.S. essential tremor patients. Those with ET have a higher prevalence of comorbidities and psychiatric disorders, both of which further complicate disease management. This study aims to stress the mental and financial budget essential tremor patients face in comparison to those without. More research is still be done in this disease state, and more attention should be spent on this population to great improve their health outcomes. To aid in this endeavor, industry pharmacists could be more involved with the financial worry those with ET patients face. For example, industry pharmacists could prioritize more affordable therapy marketing to physicians, or they could become more involved with the research and development side of ET management. In summary, patients diagnosed with ET are concurrently diagnosed with mental, physical, and financial burden that we, as future pharmacists, can resolve.

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Flavonoid Compounds and the Therapeutic Potential of Asthma Treatment

Summary By: Jay Sheppard, Pharm.D. Candidate

Asthma is a chronic condition in which an individual's normal activity, quality of life, and socioeconomic status are directly affected by the disrupted physiology of their lungs. There is a prevalence of around 300 million people worldwide, and the larger demographic of the affected population are females. For treatment of asthma, there are several medication options available that serve as the principle treatment regimens that are prescribed by physicians. Despite their efficacy, these medications present several undesirable side effects.1 Flavonoid compounds are being developed as the potential therapeutic for asthma that will avoid side effects seen by currently used medications and improve adherence.

The use of natural substances, such as flavonoids, in the pharmaceutical industry has become significantly more common. Flavonoids consist of chemical structures like phenolic rings, carbon skeletons, and multiple hydroxyl groups that allow these compounds to act as multi-target drugs.1 The benefit of flavonoid compounds in asthma are due to the anti-inflammatory mechanisms associated with their ability to act as antioxidant mediators. Flavonoids disable reactive oxygen and nitrogen species that mediate and signal an inflammatory response in the lungs. However, there is research suggesting that there are several interactions with flavonoids in the body that reduce anti-inflammatory responses such as cyclooxygenase 2 inhibition, induction of transcription factor NRF2, and induction of other transcriptional factors.1 As with the majority of most medicinal substances, bioactivity and associated health benefits of flavonoid compounds are dependent on the route of administration, phytochemical properties, absorption rates, and interactions with other compounds.1 Subsequently, flavonoids have a low bioavailability after oral administration. Research of controlled flavonoid release systems are being conducted in order to increase the bioavailability and decrease frequency of administration. Some examples of controlled release systems being studied include microemulsions, nanoparticles, and micelles. One of the major dietary flavonoids, Quercetin, was used in preclinical studies to determine the efficacy of microemulsions as a controlled release drug delivery system. As a result, these preclinical studies concluded that this mode of drug delivery demonstrated potent anti-inflammatory activity in the alveolar tissue compared to the free from of Quercetin.1

Preclinical studies are essential to determine the use of flavonoids in asthma treatment. These studies are responsible for determining the value of flavonoids combined with controlled release systems and provide a comparison of results with the flavonoid compounds without addition of controlled release systems. This responsibility is emphasized and the results show whether the controlled release systems identified allow for improved therapeutic benefit to a person with asthma. In addition, the inclusion of transdermal controlled release systems is being presented as route of administration that provides a novel approach to obtain continuous and prolonged release of flavonoids achieving systemic dosage.1 Unfortunately, systemic administration of flavonoids is suggestive of being less advantageous and could induce adverse effects, so the main efforts of preclinical studies are to compose a medication that is administered intranasally or via inhalation. They are intended to have a local effect and low systemic side effects.1 Furthermore, as preclinical trials progress in the future, the investigation of flavonoid formulations and their benefits is valuable when translating results to successful asthma treatment.

This topic of new therapeutics and drug delivery systems for asthma patients has potential for application in many areas of a pharmaceutical company that an industry pharmacist may be involved with. For an industry pharmacist, this article influences their perspective of new options that can be presented to patients with asthma. For a pharmacist in the clinical development, this article can provide supplemental information on flavonoid compounds and their use in asthma treatment. In regulatory affairs, the article can be a citation of information for their submission of an New Drug Application for their respective company. For a pharmacist discussing the benefits of a medication containing a flavonoid compound to a physician, this article can provide information about mechanisms of flavonoids that is transmittable when discussing benefits of a drug or results from clinical trials. Industry pharmacists can utilize this article to provide information that is necessary in contributing to the roles of their position.

References

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A performance evaluation framework of public health distribution for essential medicines

Summary By: Itunuoluwa D. Talabi, Pharm.D. Candidate

I. Introduction

The researchers explained that distribution network design (DND) is used as a tool to deliver essential medicines to varying healthcare facilities. Distributions networks are evaluated based on two metrics, cost and service. The challenge that most healthcare facilities face is striking a balance between the two as there are tradeoffs in both scenarios. An organization devoting more resources to the complexity of the DND forces inventory and handling costs to increase. Conversely, with cost-efficient approaches, the quality of services suffer which directly impact the patients' health outcomes. The writers argue that DND use in public health is observed from a different perspective than traditional commercial organization. DND is affected by social motives and prejudices in addition to cost. The author's objective in this article is to evaluate the performance and value of public health distribution networks (PHDNs) in distribution network design for receiving essential medicine and develop a step-wise performance evaluation process of PHDNs that can be used across Indian states and other developing economies [1].

II. Methods

The 28 states in India encompasses both urban and rural public health facilities broken down into primary, secondary and tertiary levels (Fig. 1). Tertiary levels include best care involving specialized medicine, whereas primary level includes subcenters and primary health centers. The researchers elected to use all six major patterns of PHDNs with two to four echelon networks (Table 1). Each echelon is representative of a step, making the distribution process more complex. For example, Pattern 1 is a two-echelon network where the suppliers directly supply medicine to district warehouses and then ship to healthcare facilities. Whereas, Pattern 6 is a four-echelon network with suppliers delivering to state warehouses first, then regional warehouses and then district warehouses. The fourth step being delivery of medicine to the health facility.

When evaluating the six distribution patterns, variation is also attributed to both population density and health index. The range of data led to the division of states based on three categories, high, medium and low for both. The researchers developed an algorithm that displays the base design of PHDN which encompasses all six variant patterns of PHDNs (Fig. 2). The base design includes demand for drugs, process flow and physical flow. Additionally, frequency of orders, supply of essential medicines and delivery of essential medicines were assessed.

After the base design was synthesized, a hierarchy of PHDN evaluation was created into two levels. The first level being cost and service criteria. The second, included sub criteria. Inventory, transportation, handling and information system costs were attributed to cost. Response time, availability, facility experiences, order visibility and returnability was associated with services (Fig. 3).

The evaluation of PHDNs based on the identified nine criteria involved using a 7-point Likert scale. Experts familiar with PHDNs were contacted to answer a questionnaire with the assigned values 1 for extremely poor and 7 to extremely good. An online meeting with the experts was moderated by one author to mitigate inconveniences. The experts were meant to reach a consensus for each rating. The next step required the determination of factor scores for all the sub-criterion. Researchers computed this value by multiplying the score obtained from sub-criterion and the score associated with level of importance. Lastly, a composite score was given by the summation of factors scores respective to the PHDN. Those that accrued the highest total factor score ranked 1, and the rest followed (Table 9).

The framework of PHDN was evaluated separately using a “cost-service matrix” using the previous information gathered (Fig. 4).

III. Results

The findings of this study showcased a significantly higher level of importance of the service factor as opposed to the cost factor. The weight of the components of the cost factor and service factors were consistent with this insight. T.N PHDN was the best-performing in terms of service. Punjab PHDN ranked the most cost-effective option. The poor performance of Bihar PHDN was revealed to be due to shortages, irregularities between facilities and generally poor patient experiences. States that used three-tier to four- tier network PHDNs were ones that mostly had a decent level of performance of the service criteria. Bihar PHDN was an exception to this rule. Punjab PHDN scored best for cost due to few regional warehouses and consequently, less inventories to be maintained.

IV. Conclusion

The study was able to achieve a base design of PHDNs to be utilized as a metric for multiple states in India and other developing countries. In addition, the performance evaluation criteria was created using the 7-point Likert scale to better conceptualize the data. Moreover, researchers introduced a cost-service matrix to be used simultaneously against the performance criteria. The data allowed for understanding which PHDN was best for service or cost, both or neither. This information can be used for public health policy makers to know what to include to create a balanced and streamlined PHDN to increase access and quality of essential medicines.

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The Role of Data and Safety Monitoring Boards in Clinical Trials

Summary By: David Yi, MBA, Pharm.D. Candidate

The use of clinical trials to evaluate the benefits and risks of medical interventions is an ethical imperative, but unexpected outcomes can occur. Protecting the welfare of participants in clinical trials through the monitoring of trial results is an important aspect of clinical research. One such way is through the oversight of Data and Safety Monitoring Boards (DSMBs). In his article "Independent Oversight of Clinical Trials through Data and Safety Monitoring Boards," Scott R. Evans highlights the importance of DSMBs in the clinical trial process and presents the history of DSMBs, from their conception in the Greenberg Report in 1967, to their use in the Coronary Drug Project, to their current widespread use in clinical trials.

DSMBs are critical to the success of clinical trials. They provide independent oversight to ensure the safety of the trial participants and the integrity of the data. They monitor the progress of the trial, review the data, and make recommendations for the continuation or discontinuation of the trial. DSMB members are field experts not involved in the day-to-day operations of the trial. This separation of duties helps to ensure that the DSMB remains unbiased and independent. Evans describes the Cardiac Arrhythmia Suppression Trial (CAST), a randomized placebo-controlled trial (RCT) that evaluated the effects of three drugs on sudden cardiac death or all-cause mortality in patients after a myocardial infarction. After 2 years, the DSMB recommended discontinuation of the encainide and flecainide arms following evidence of increased mortality, demonstrating the importance of DSMBs in preventing harm to participants while ensuring the validity of clinical trial results.

The concept of DSMBs was first introduced in the Greenberg Report, commissioned by the U.S. National Heart Institute, which recommended an Advisory Committee of senior experts in the field of study but not data-contributing participants who could remain dispassionate and separate from investigators with a stake in the trial outcome. The report also recommended the development of a mechanism for early termination should unusual circumstances determine that a study should not be continued. The termination of a study must be based on careful analysis of the advice and recommendation of the committee consultants.

The Coronary Drug Project (CDP) was one of the first major trials overseen by a DSMB. The CDP was a randomized, double-blind, placebo-controlled trial evaluating five lipid-modifying agents against placebo for men with a previously documented myocardial infarction. While the CDP had a steering committee of investigators, it did not have a trial monitoring committee and CDP investigators were informed of accumulating outcome data. Following the Greenberg Report, investigators were restricted from outcomes data to prevent biased decisions and a safety monitoring committee was formed to regularly review the data. The committee eventually recommended termination of several active treatment arms during the trial due to adverse events or insignificant efficacy.

Evans emphasizes the importance of DSMBs in protecting participants in clinical trials and ensuring the validity of trial results and the safety of clinical trial participants, highlighting several key features of DSMBs, including their independence from the trial sponsor and investigators, their access to interim data, their ability to make recommendations based on the data, and their obligation to report their findings to the trial sponsor and the FDA. DSMBs are typically composed of a small group of experts who are not involved in the conduct of the trial and have no financial or other conflicts of interest. As the DSMB's main responsibility is to protect the safety and welfare of trial participants, they have unrestricted access to all unblinded data to make informed decisions. Without DSMBs, there would be a risk of harm to participants and the results of clinical trials would be open to bias and manipulation. The use of DSMBs has become standard practice in the clinical trial process and is a critical component of ethical and scientific research. The DSMB provides an independent evaluation of the trial data, which is crucial for ensuring that investigators and sponsors do not have access to ongoing trial results to prevent biased decisions on their part.

In conclusion, Evans stresses that the use of DSMBs is essential to the success of randomized clinical trials. The role of the DSMB is to protect the welfare of trial participants and ensure the validity of trial results. The use of DSMBs has become standard practice in the clinical trial process and is a critical component of ethical and scientific research. As demonstrated by the Cardiac Arrhythmia Suppression Trial and the Coronary Drug Project, DSMBs have played a crucial role in preventing harm to participants and ensuring the validity of trial results.

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