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Centralized access to cancer registries

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Abstract

Purpose: The U.S. Food and Drug Administration and National Cancer Institute are seeking to improve methods to evaluate cancer as a clinical outcome in postapproval studies of drug and device safety. Challenges to monitoring cancer outcomes include years-long latency periods for many cancers, difficulty in tracking patients over long periods of time, missing outcomes of interest if relying on reporting by patients or health care providers, burden of collecting high-quality, detailed documentation of incident cancers, and low statistical power for rarer cancers.

Methods: Registration of incident cancers including patient identifiers occurs in every U.S. state. Yet, each state cancer registry is administered and must be accessed separately, which creates a nearly insur-mountable burden of time, effort, and cost for postmarket surveillance in multiple or all states. A voluntary process is in development which would allow states to reduce these barriers and enhance the health and safety of their residents. Called the Virtual Pooled RegistryeCancer Linkage System, state cancer registries will continue to hold and control their registry data while having access to a more streamlined process for postmarket surveillance, providing better quality, complete, and more rapid discovery.

Results: A Web-based application and review process are in development with an additional effort devoted to highly automated linkage processes and federally compliant data file transmission security.

Conclusions: The Food and Drug Administration and National Cancer Institute will have enhanced abilities to perform high-quality postmarket surveillance and other research at lower cost and with faster speed. This system also seeks to reduce cost and burden by participating state cancer registries. This process also supports the current modifications proposed by the U.S. Department of Health and Human Services and 15 other Federal Departments and Agencies to modernize, strengthen, and make more effective the Federal Policy for the Protection of Human Subjects known as the Common Rule.

Keywords

Carcinogens; Neoplasms; Pharmaceutical preparations; Registries; United States Food and Drug Administration

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Introduction

Evaluation of human carcinogenic potential associated with drugs or devices is challenging due to the long latency period associated with most cancers and is not feasible in most premarket assessments. Although evidence from animal studies or biochemical properties may provide some reasons to monitor cancer among patients receiving a drug or device, clinical trials are necessarily too short to assess cancer risk. The U.S. Food and Drug Administration (FDA) is seeking opportunities to improve postmarket surveillance methods, including efforts within the Center for Devices and Radiological Health [1] with a focus on cancer, in conjunction with the National Cancer Institute (NCI) [2]. Conventional methods for long-term postmarket surveillance may resemble cohort studies, with the substantial cost and effort required to maintain current contact and address information on patients for many years and, often equally challenging, to obtain notification of outcomes of interests and collect high-quality clinical documentation. In contrast, because fully identified cancer surveillance is active in every U.S. state, national cancer incidence monitoring already exists and is based on high-quality medical record documentation. This system of cancer registration provides a well-developed existing platform for postmarket surveillance of cancer outcomes.

Sponsored by the FDA and NCI, a 2-day public meeting was convened in September, 2014, to discuss methodologic challenges and identify opportunities entitled “Methodological Considerations in Evaluation of Cancer as an Adverse Outcome Associated With Use of Non-Oncological Drugs and Biological Products in the Postapproval Setting” [3]. A model to create an efficient platform for postmarket surveillance of cancer outcomes which leverages the state and federal investment in cancer surveillance is presented here.

Methods

Cancer surveillance in the United States is a system of individual state registries which together comprise a complete collection of cancer incidence across the country. Although administratively separate, a high degree of standardization exists including a broad set of well-defined data elements including cancer site and histology, date of diagnosis, stage, prognostic factors, initial course of treatment, and mortality. Common standards and procedures for quality control and completeness have been adopted [4]. Each state has enacted a legal mandate [5] for cancer reporting, and the collection and use of the registry data are exempt from Health Insurance Portability and Accountability Act patient authorization requirement. Each reportable case record includes patient identifiers to allow identification and consolidation of multiple reports of the same tumor and to support epidemiologic and other research. All state cancer registries report to either the NCI’s Surveillance, Epidemiologic and End Results program [6], the Centers for Disease Control and Prevention through the National Program of Cancer Registries [7], or both. In addition, all states, regardless of funding source, report information to the North American Association of Central Cancer Registries (NAACCR) [8] for certification and publication of aggregate data purposes. However, none of these multistate organizations have access to patient identifiers.

Thus, although state cancer registries are an invaluable resource which could serve to monitor cancer incidence among persons receiving FDA-approved drugs or devices, to do so requires collaboration with each state separately. Furthermore, the application process differs for each state, thus requiring approximately 50 unique sets of requirements for review and approval of each linkage study protocol. This poses a significant burden and cost as well as lengthy delays for all multistate or national studies. Some of these difficulties were described by researchers attempting to conduct a single research linkage with each state cancer registry who identified several barriers to this system including excessive amounts of time involved trying to obtain institutional review board (IRB) approval from each state (over 700 hours for 22 states), complicated approval processes, high costs, temporal differences among the registries, and registry difficulty in performing linkage studies [9]. All these factors contribute to the high cost and inefficiency of conducting cancer research and postmarket surveillance with state-based cancer surveillance data.

With coordination and state approval, an efficient national postmarket surveillance process can be achieved in the United States. There is growing interest in “virtually” pooling data across geopolitical boundaries to simulate a multistate cancer research database with all the appropriate safeguards to maintain the privacy of the cancer patient and the rights and ownership of the data by the states. This voluntary virtual pooled registry cancer linkage system (VPR-CLS) will serve as a federated research database of participating registries, while still allowing each individual state to fully control their registry data. The National Center for Health Statistics National Death Index [10] is an example of a centralized database that allows researchers simultaneous access to data from all states via a single application and data request process, while maintaining adherence to applicable policies and regulations assuring appropriate protection of confidentiality. Unlike the National Death Index which collects and aggregates identified mortality data into a central database, with the VPR-CLS, each state’s cancer registry data will continue to remain behind the registry firewall, yet research linkages can be performed with multiple states simultaneously and with a streamlined application process. The federal Cancer Research Network’s Virtual Data Warehouse [11] has demonstrated the feasibility of this approach.

Initiated in September, 2015, the VPR-CLS is administered by NAACCR and will support postmarket surveillance studies as well as other cancer epidemiology research. Participation of cancer registries and researchers is entirely voluntary. To assure efficiency, the VPR-CLS will establish a Linkage Coordinating Center to administer the program and support the needs of FDA, industry/researchers, and state cancer registries. A standard application process will be developed with oversight and review by a Research Review Committee. A fee structure will be established to support the infrastructure and registry linkage experts will develop a uniform linkage protocol to maximally automate the linkage process and eliminate methodologic variation. Funding will be sought to provide support to each participating cancer registry. Technical assistance will be provided by the Linkage Coordination Center to assure that data from each postmarket surveillance and other research project are provided and standardized in a manner that will maximize the likelihood of linkage success. An overview (Fig. 1) of the proposed process is:

- Linkage Coordination Center provides documentation to participating cancer registries for annual linkage file preparation
- Web-based postmarket/research application
- Research Review Committee review and approval
- Linkage Coordination Center assists researcher with linkage file preparation
- Linkage Coordination Center securely transmits the research file to all participating registries
- Participating registries perform highly automated linkage behind the registry firewall following a uniform procedure
- A standard tabular report of the frequency of matches (de-identified) by incidence year is transmitted to the Linkage Coordination Center for release to researcher
- Using the frequency report, the researcher decides which registries to approach to initiate institutional review board approval for access to patient identifiers, data release, and data use agreements.

This process will support repeated monitoring over time of a fixed cohort of patients entered into a postmarket surveillance study as well as a dynamic roster with new patients added periodically.

Discussion

The VPR-CLS creates an unprecedented resource to support postmarket surveillance, cancer researchers, and public health officials while leveraging the value of state cancer registries and improving cancer control and prevention. Currently, studies performing multiple state cancer linkages are not able to standardize the linkage methodology from state to state, introducing undesirable methodologic differences. The proposed approach will facilitate more rigorous scientific research by adopting a standardized methodology. The VPR-CSL will also be developing a centralized application and approvals process that state cancer registries may find useful. Furthermore, development of a central IRB dedicated to the VPR-CLS is being considered which supports the proposed modifications proposed by the U.S. Department of Health and Human Services and 15 other Federal departments and agencies to modernize, strengthen, and make more effective the Federal Policy for the Protection of Human Subjects known as the Common Rule [12]. These proposed modifications also attempt to strengthen the effectiveness and efficiency of the oversight system by making the level of review more proportional to the seriousness of the risks and seeks to avoid requirements that do not enhance protection and impose burden, which can decrease efficiency, waste resources, and erode trust. This includes a proposal to mandate that U.S. institutions engaged in cooperative research rely on a single IRB, with certain exceptions. The government notes that cumbersome and outdated regulatory standards overwhelm and distract institutions, IRBs, and investigators in ways that stymie efforts to appropriately address the real risks and benefits of research. These methods would reduce the costs to state cancer registries as well as researchers and industry.

Conclusion

Given the long latency period recognized for many cancers, methods for postmarket surveillance of drugs and devices for cancer outcomes can be substantially improved, while reducing cost, effort, and delay. Although complete cancer incidence reporting occurs across the United States, a unified national database including personal identifiers does not exist. Thus far, conducting multistate or national postmarket surveillance leveraging existing cancer registry data requires a daunting and expensive application and approvals process with at least 50 registries and introduces inconsistent methods for identifying cancer outcomes. Now, an infrastructure is being established which will create the capacity for monitoring cancer incidence simultaneously in all states which choose to participate, providing the capacity for earlier discovery of elevated risk, even among rare cancers and at lower cost and societal burden. Decisions on and control of personally identifiable data release will remain with each state registry.

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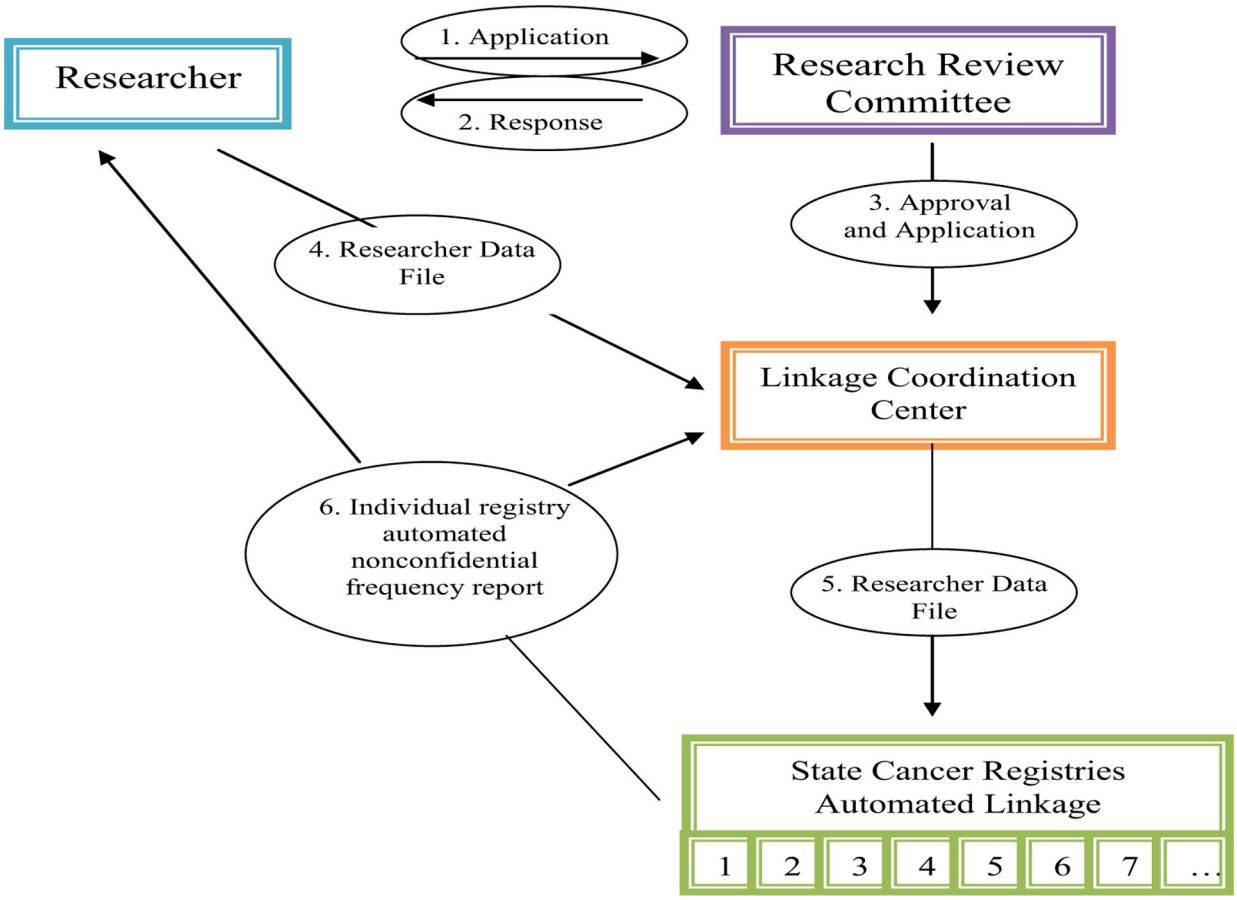

Fig. 1.
Virtual pooled registry e cancer linkage system.