

# Commentary on Point-of-Care Clinical Trials in Sports Medicine Research: Identifying Effective Treatment Interventions Through Real-World Evidence

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The technical note of Lam et al<sup>1</sup> on the pragmatic or point-of-care clinical trial (POC-CT) design offers valuable insights into a nascent area of research in athletic training. Although the authors did an excellent job detailing the role and advantages of and considerations for the POC-CT design in athletic training, the introduction of the POC-CT is a small component of a growing approach across health care using information from “real-world” encounters for evidence generation. This approach, known as *Real-World Evidence* (RWE), could lead to novel applications of health care delivery and evidence generation. This commentary is intended to provide the athletic training profession with a brief, but not all-inclusive, introduction to RWE and how athletic trainers (ATs) can (1) improve the overall quality of care and (2) position the athletic training profession to better participate and contribute within the larger health care ecosystem.

## What is RWE? How is it Generated?

A number of definitions have been used to define RWE.<sup>2–5</sup> However, these definitions focus on patient information obtained from data collected outside of the traditional research setting to generate evidence about the effectiveness of clinical care and patient outcomes.<sup>2,3</sup> Although some sources, such as the POC-CT, are designed to use real-world data to answer a specific research question, other sources may include electronic medical records (EMRs), patient-generated health data (eg, mobile health technologies and wearables), patient registries, and medical claims, among others that are traditionally associated with clinical care.<sup>4</sup> These alternative data sources may be used as secondary sources of information for evidence generation. In essence, data captured at the point of care through routine clinical interactions and stored in an EMR, medical claims associated with billing for patient care, and even patient-reported outcome measures generated by individuals via mobile health apps could be used to improve health care delivery and outcomes.

A variety of methodologic approaches, including both experimental and observational study designs, can be used to generate RWE.<sup>6</sup> Athletic training research incorporates a number of these study designs, but they may not currently be used to generate RWE. Similar to the many study designs available, a multitude of outcomes and use cases are available for real-world data to generate RWE.<sup>2,4,7</sup> Athletic training's

push for more use and dissemination of patient-reported outcome and health-related quality-of-life measures could become key to the future generation of athletic training RWE.

## Lessons From Other Health Care Disciplines

The passage of the 21st-Century Cures Act<sup>5</sup> has placed an emphasis on accelerating the pace of discovery and innovation of health care delivery methods to patients. Included in the 21st-Century Cures Act is the section “Modern Trial Design and Evidence Development,” which addresses RWE. This has helped to facilitate a new framework from the Food and Drug Administration (FDA) on the potential use of RWE in regulatory decisions about drug development and approval.<sup>3</sup> Advantages of RWE include reduced costs and time to evidence generation compared with traditional randomized clinical trials. Currently, it can take years for a drug to receive approval (ie, preclinical, clinical, and new drug application review phases). Reducing the time and costs associated with drug development and approval could allow more patients access to better or novel treatments.

Additionally, the FDA conducts postmarket surveillance on drugs and medical products by leveraging RWE via the Sentinel System,<sup>8</sup> which focuses on safety surveillance. In orthopaedics, the safety and adverse events associated with medical devices or surgical procedures may ultimately affect the delivery of care to athletes. A previous approach<sup>9</sup> that identified adverse events from hyaluronic acid injections and the time to knee replacement surgery may provide insights into how RWE can be used for safety surveillance relative to athletic training. Understanding the types and frequencies of adverse events will permit regulatory or clinical decisions to be made regarding future use as part of recommended care.

Pharmaceutical research has focused on the development and implementation of personalized, or precision medicine, for individuals.<sup>10</sup> *Precision medicine* addresses a targeted individualized treatment response rather than an average response from a cohort of individuals in a clinical trial. This is often done by using advanced analytical approaches to study individual characteristics from personal health and genomic information. Then, RWE can be used to predict individual risk or optimal treatment therapies or pathways to maximize an individual's outcomes and reduce the risks associated with the treatment.

Another growing trend across health care focuses on the interoperability and linkage of multiple types of data sources. The development of common data models (CDMs; eg, the National Patient-Centered Clinical Research Network CDM [pcornt.org], Sentinel CDM [https://www.sentinelinitiative.org/sentinel/data/distributed-database-common-data-model], Informatics for Integrating Biology & the Bedside [https://www.i2b2.org], and Observational Medical Outcomes Partnership CDM [https://www.ohdsi.org/data-standardization/the-common-data-model/]) has provided a foundation for leveraging data to generate RWE. Standardizing data in a CDM allows for the integration of disparate real-world datasets to provide increased interoperability across data sources or the ability to link multiple data sources for future research that may not currently be possible. Understanding where and how data can be standardized may create opportunities for ATs to engage in select research networks.

### **Real-World Evidence and ATs: Why Do We as Health Care Professionals Need RWE?**

Evidence generation falls along a continuum based on the methodologic approaches that can be used to support clinical decision making and best practices. As ATs continue to embrace and implement evidence-based practice, we must understand the multiple forms of evidence generation necessary to contextualize findings from different types of research. Lam et al<sup>1</sup> did a good job detailing the strengths and limitations of randomized clinical trials, the POC-CT, and observational studies. However, evidence from different methodologic approaches should not be viewed in isolation as individual silos but rather in a more translational context. Randomized clinical trials may help establish efficacy specific to an intervention, but ATs work with individuals in the real world. Clinical trials often have strict eligibility criteria, which may not reflect the true population and could influence how effective treatments are in routine clinical care. As many ATs work with patients or athletes with comorbidities, RWE allows for a better understanding of the generalization of therapeutic interventions. Conversely, observational RWE approaches could generate research hypotheses or be implemented to identify targeted cohorts for future clinical trials.

Also, RWE allows data to be viewed longitudinally. Information from EMRs can provide clinicians with an individual's entire medical history and interactions with the health care system. Accessing data across multiple years, including routine patient-reported outcome measures throughout an athlete's career, could provide insights into the long-term consequences of athletic injuries.

Finally, health care is transitioning from a pay-per-service model to a more value-based approach. As a result, RWE provides a unique opportunity to answer questions about costs associated with clinical care by using health economics and outcomes research. Understanding the financial aspects of health care delivery and services could help ATs with resource utilization and providing cost-effective treatment interventions for patients.

### **Real-World Evidence in Athletic Training: What are the Barriers?**

The full potential of RWE is still emerging. Special considerations are warranted regarding data quality and governing restrictions and regulations before implementing

RWE research. Currently, the data collected by clinicians and entered into EMRs are not commonly input in ways that support research. These may include individual user concerns about data entry (missing or incomplete data and use of unstructured clinical notes) and systematic concerns (multiple EMR vendors and lack of interoperability) when investigators attempt to conduct large-scale studies across multiple sites. Data and human participant protection and privacy concerns will still require institutional review board oversight to ensure compliance with the Health Insurance Portability and Accountability Act and part 11 of the Code of Federal Regulations Title 21 (ie, electronic signatures and records).<sup>11</sup> International governance regulations, such as the European Union General Data Protection Regulation, may also apply.<sup>12</sup> These regulatory, privacy, and data-protection concerns may ultimately affect and determine data availability and accessibility for or research methodologic approaches to RWE in athletic training settings.

Furthermore, a number of potential athletic training RWE applications, including the proposed POC-CT, will involve practicing clinicians. This could ultimately increase the burden on these individuals to engage and participate in RWE generation. The necessary education and training, time commitment, and incentives for participation will need to be considered and addressed before implementation.

Data availability is also a potential limitation, especially when considering health economics and outcomes research. These outcomes are traditionally based on a combination of claims data and EMR or additional data (eg, laboratory reports, imaging, and medications) and may not be available to most practicing ATs. Although cost- and value-based associated research could be of great benefit to the profession, it may be limited to select applications in orthopaedic centers or university academic medical centers.

### **Real-World Evidence in Athletic Training: What do We Already Have in Place?**

Some examples are either readily available or could provide a framework on how to incorporate RWE in athletic training. The Datalys Center for Sports Injury Research and Prevention, Inc (Indianapolis, IN), with contributions from ATs, illustrates how data from clinical care can be used to identify epidemiologic trends across athletic training at scale. The limitation to this approach is the narrow scope of data that can be collected and the resulting type of evidence generated. However, increased value from this approach is possible when injury-surveillance outcomes are used to determine the effects of policy and rule changes on safety during athletic participation.<sup>13</sup>

The POC-CT, with an integrated EMR across all participating Athletic Training Practice-Based Research Network clinical sites and mobile patient-reported outcome measures reporting introduced by Lam et al,<sup>1</sup> provides multiple components for generating RWE. The POC-CT uses an experimental RWE approach. Integrating patient-reported health data generated outside of routine clinical visits adds longitudinal information that can be leveraged by ATs.

The POC-CT also targets comparative effectiveness outcomes,<sup>1</sup> which can be used to compare the effectiveness of multiple treatments or the costs associated with either treatments or care delivery. The latter approach emphasizes health economics and could be an asset in understanding cost-affordable or cost-alternative treatment options, along with

transitioning athletic training toward a value-based approach to clinical care.

Injury and illness prevention and wellness promotion is 1 of the 5 domains of the Board of Certification practice analysis.<sup>14</sup> Although injury-prevention research can be conducted using a variety of methodologic approaches, the cluster randomized controlled trial is another experimental design that can be used to generate RWE.<sup>6</sup> This approach has been used in athletic injury-prevention research on ankle bracing<sup>15,16</sup> and more recently to assess the FIFA 11+ Injury-Prevention Program.<sup>17</sup> A better understanding of how and when this study design could be used in athletic training may lead to future RWE applications.

Lastly, prospective observational studies offer advanced analytical approaches for developing injury-prediction models for lower extremity and core injuries in athletic training.<sup>18,19</sup> Advanced analytics may be used in the future to predict injury risk as well as in precision medicine to target specified treatments with the goal of maximizing patient outcomes.

### Real-World Evidence and Athletic Training: Where Do We Go From Here?

Numerous opportunities are available for ATs to generate RWE. However, not all ATs are positioned to leverage all aspects associated with RWE. The Strategic Alliance Research Agenda Task Force has identified areas of emphasis in athletic training where RWE could be of value.<sup>20</sup> Multiple stakeholders should be collectively engaged across the profession to determine the value, effect, and role RWE could have on athletic training. This could provide ATs with recommendations on how RWE might be leveraged to address some of these key areas. Additionally, ATs can continue to educate about and encourage researcher-clinician engagement and collaborations to foster relationships for future RWE opportunities. Finally, ATs should look at how RWE is currently being used throughout health care to better understand the emergence and importance of this approach.

Health care is currently in a state of transition, but the use of and emphasis on RWE is growing. As ATs continue to contribute to overall health care knowledge, an understanding and eventual pursuit of RWE is warranted. Athletic trainers are uniquely positioned in health care to contribute to RWE generation. Adopting and implementing appropriate RWE approaches could position ATs as significant contributors in health care.

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