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## Using Big Data to Mimic a Clinical Trial

**How analytical expertise extracts the highest value from Alberta cancer data**

Randomized controlled trials (RCTs) are the gold standard of study design when evaluating a new cancer drug or treatment. In RCTs, researchers randomly assign participants to receive one therapy or another, to compare the relative effectiveness. While very valuable, such clinical studies are not always feasible to conduct because they can be too expensive to run, can last decades, or may not be ethical.

Now a team of researchers in Alberta believe they've proven that equally accurate conclusions can be drawn more quickly and easily, without needing to interview and track patients face to face over months or years. Instead, they're analyzing real-world evidence already collected and stored in vast provincial cancer databases.

*Dr. Winson Cheung*

"Our goal is not to replace an RCT, which is still the ideal study design for testing new interventions" says Dr. Winson Cheung, Provincial Director of Health Services Research & Real-World Evidence within Cancer Research & Analytics (Cancer Care Alberta). He also leads the Oncology Outcomes (O2) program. His team's paper was recently published in JAMA Network Open.

"If a trial can be done, then yes, we should still do it. But sometimes these RCTs are not feasible, or in the case of treating young children, for example, it's not ethical to wait 10 years for results. What we set out to prove was whether studying real-world data could allow us to mimic or mirror the design of a randomized controlled trial, without actually doing one."

The team hypothesized that if they applied all of the rigourous standards and conditions employed in an existing RCT to the specific dataset they were analyzing – and ended up with the same results – that would demonstrate their method of analysis was scientifically sound.

The approach is called "target trial emulation", and relies on huge databases containing diverse health information about many people. Alberta has several administrative databases; combined with the analytical expertise to interpret them, they provide real-world evidence to support better clinical decision-making, quality improvement, and cancer research.

Dr. Devon Boyne, clinical epidemiologist and O2 Assistant Director, led the project.

*Dr. Devon Boyne*

"In many oncology settings, the decision to initiate one treatment strategy over another is often based on physician and patient preference rather than findings from a phase III randomized clinical trial, especially if there are no RCTs comparing newer treatment options head-to-head. In these situations, conducting observational analyses of real-world data can help physicians and patients make more informed decisions regarding their optimal course of treatment."

To test the method, Boyne, Cheung and their colleagues chose as their target trial a well-established study called the International Duration Evaluation of Adjuvant (IDEA) trial. Using highly-specific eligibility and other criteria from the IDEA study, they used real-world data from patients already treated in Alberta to examine the effectiveness of a shortened period of chemotherapy for stage III colon cancer patients. The findings were compared against other previous observational analyses which yielded conflicting conclusions.

Not only did the analysis produce the same results as the original IDEA trial, it revealed shortcomings in the methodology used by researchers in the other conflicting observational studies.

"The IDEA trial was a well-designed trial," says Cheung. "The goal of our paper was to reassure us and provide evidence that using the target trial emulation approach to analyze real-world data can give comparable findings to that of a randomized trial. It can be a scientifically valid option when an RCT is not feasible."

For the authors, the bottom line is clear and signals a new era in the use of 'big data': target trial emulation can help to provide complementary real-world evidence in situations where a randomized controlled trial is not possible or where there are lingering concerns about the generalizability of such findings to real-world patients. That is, with two important caveats.

First, available cancer databases need to be large, and allow for linkage with administrative data to include information on diagnoses, treatment pathways, health system usage, and survival. Second, significant clinical and analytical expertise is required in order to draw appropriate conclusions from that data.

"We're very fortunate here in Alberta," notes Cheung. "We have a single health authority, as well as well-trained, advanced-level statisticians including those within Cancer Care Alberta's Surveillance & Reporting group, who can comb through the health data and make sense of it. They know the data intimately, can gather it appropriately and can manipulate it for analysis. We also have a plethora of clinicians who can provide input. Without that analytical prowess and clinical knowledge, the data wouldn't mean anything. As a result, we are doing things that are ahead of the curve compared to many other jurisdictions and centres."

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**Sources:**

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