When Human Behavior Challenges the Data: Strategic Interaction and Response Shift as Threats to Validity in Clinical Research

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ABSTRACT

In clinical research, the validity of results may be compromised by classical factors such as bias, confounders, and sampling error. However, other factors related to human behavior, which are not always considered, can also undermine conclusions. This paper explores two phenomena: *strategic interaction* and *response shift*. The first occurs when individuals adjust their behavior based on what they believe others will do. The second involves a change in how individuals assess their own health over time. Through everyday examples —such as penalty kicks in soccer, traffic decisions, or self-reported quality of life— we analyze how these dynamics can impact the validity of studies. Recognizing them is essential for better interpreting results and designing methodological strategies to minimize their impact.

Keywords: strategic interaction; response shift; internal validity; external validity; behavioral bias

Cuando el comportamiento humano desafía los datos: interacción estratégica y cambio de respuesta como amenazas a la validez en investigación clínica

RESUMEN

En investigación clínica, la validez de los resultados puede verse comprometida por factores clásicos como los sesgos, los confundidores y el azar de muestreo. Sin embargo, hay otros factores vinculados al comportamiento humano, que no siempre se contemplan y pueden comprometer las conclusiones. Esta nota explora dos fenómenos: la interacción estratégica y el cambio de respuesta (*response shift)*. El primero ocurre cuando las personas ajustan su conducta en función de lo que creen que harán los demás. El segundo implica una modificación en la forma en que las personas evalúan su propia salud a lo largo del tiempo. A través de ejemplos cotidianos, como los penales en el fútbol, las decisiones de tránsito o los autoinformes de calidad de vida, analizaremos cómo estas dinámicas pueden afectar la validez de los estudios. Reconocerlas es clave para interpretar mejor los resultados y diseñar estrategias metodológicas que las minimicen.

Palabras clave: interacción estratégica, cambio de respuesta, validez interna, validez externa, sesgo de comportamiento.

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INTRODUCTION

In clinical research, the quality of evidence largely depends on study validity. Internal validity refers to whether the results accurately represent the reality of the phenomenon under study. In other words, it addresses questions such as: *Am I measuring what I intend to measure? Am I measuring it correctly?* External validity, in turn, refers to the generalizability of the study findings to other populations or contexts. An important principle is that external validity depends on internal validity. It is not possible to generalize results from a study that is not valid in its original context. If what was measured was incorrect, extrapolation lacks a sound basis[1].

Among the classic factors that threaten validity are bias, confounding, and sampling variability[1]. Selection bias occurs when the participants included in a study do not adequately represent the target population. For example, if we seek to evaluate healthy habits but select only individuals who attend a gym, we would be starting from a sample with behaviors already oriented toward health, thereby biasing the results. Another common type of bias is information bias, which arises from systematic errors in data collection or measurement, such as when assessment instruments lack precision or questions lead respondents toward certain answers[2].

Although these phenomena have been widely explored in the literature, there are other, less frequently discussed threats related to human behavior that may—or may not—compromise study results[3].

In this note, we explore two of them: strategic interaction and response shift, phenomena that challenge our traditional ways of interpreting and predicting data.

STRATEGIC INTERACTION

Strategic interaction refers to a situation in which an individual's behavior is conditioned by what they believe others will do, and vice versa. It is a dynamic phenomenon in which each individual adjusts their decisions by anticipating the actions of others, generating a feedback loop that can alter expected outcomes[4].

This concept originates in game theory and applies to contexts in which actors' decisions are not independent but rather mutually influential[4].

Montiel and the Penalty Kick in the 2022 World Cup

On December 18, 2022, Argentinians across the country gathered with friends or family to watch the World Cup final: Argentina versus France. After an intense match and a dramatic extra time, the outcome was decided by a penalty shootout. In the fourth penalty of the series, Gonzalo Montiel stepped up to take the decisive kick. Predictions at home suggested that he would shoot to the goalkeeper's left. Why? Because the French goalkeeper typically dove to his right. Montiel knew this. However, the penalty was taken precisely to the goalkeeper's right. The prediction failed. Why did it fail? The goalkeeper also knew that Montiel was aware of his tendencies. And Montiel knew that the goalkeeper knew. And so on. This dynamic—*I know that you know that I know*—is known as strategic interaction. Both players adjusted their behavior based on what they believed the other would do. The result? Any predictable pattern was eliminated. This is a classic example from game theory: when all players act strategically, predictions may fail[5].

A Long Holiday Weekend and Google Maps® on Route 2

Let us imagine a Friday afternoon before a Carnival long weekend. We plan to travel to the Atlantic coast and, in order to avoid traffic congestion, we consult Google Maps®. The system informs us that Route 2 is clear, which seems like an excellent opportunity to leave. But are we the only ones checking Google Maps? Certainly not. Hundreds or thousands of people make decisions at the same time, influenced by the same source of information. Everyone observes that Route 2 appears clear and, motivated by that prediction, decides to leave at the same time and take the same route. As a consequence, what was initially a clear road quickly becomes congested. The original prediction ceases to be valid –not because it was incorrectly calculated, but because users adjusted their behavior in response to that prediction. In this scenario, human behavior, reinforced by trust in technology, generates a new and unexpected pattern, known as automation bias. What initially appeared to be a reliable recommendation becomes the very cause of the problem it was intended to prevent[6,7].

Surveys and Trump's Victory in 2016

In the 2016 United States presidential election, nearly all polls predicted a victory for Hillary Clinton[8]. However, Donald Trump won. What happened? Among other factors, two important biases were identified:

- **Selection bias:** many polls did not adequately represent rural or undecided voters[9].
- **Response bias:** some voters concealed their preference for Trump due to embarrassment or fear of social judgment (social desirability)[10].

However, strategic interaction may also have played a role: voters may suspect that the pollster favors Hillary Clinton and adjust their responses accordingly. In turn, the pollster may adapt their questioning based on what they believe the respondent thinks. This circular dynamic can distort the collected data and cause polling predictions to fail.

RESPONSE SHIFT: WHEN PERCEPTION ALSO CHANGES

Assuming that an individual's self-assessment of health or quality of life remains unchanged over time is a simplistic notion. While it may be statistically convenient, it is conceptually limited. Assuming that a person undergoing a complex diagnosis or treatment will maintain an unchanged perception of their health status before and after the process ignores the subjective dimension. *Response shift* refers to a different but equally

important phenomenon: a change in the way an individual evaluates their own quality of life over time. This does not reflect a true change in physical status, but rather a change in how that status is interpreted[11,12].

This change may manifest in three ways:

• **Recalibration:** the patient changes their internal scale. What was previously a "*5*" on a discomfort scale may now be perceived as a "3."

• **Reprioritization:** values or priorities change, such as shifting from prioritizing mobility to prioritizing social relationships.

• **Reconceptualization:** the individual redefines what it means to "feel well" or to "have quality of life"[11].

A context particularly sensitive to response shift is longitudinal studies that assess patient-reported outcomes. For example, a patient who begins oncologic treatment with chemotherapy may rate their fatigue as severe, assigning it a score of 7 on a scale from 0 to 10 (where higher values indicate greater fatigue). However, months later –after having experienced even more intense treatment-related effects– the patient is asked to retrospectively evaluate how they believe they felt at the beginning of treatment. This time, they rate their initial fatigue as a 4, that is, mild. This change does not reflect a retroactive clinical improvement, but rather a recalibration of the internal scale: what initially represented a 7 is now interpreted as a 4. If this phenomenon is not taken into account, the true burden of treatment-related adverse effects –such as chemotherapy-induced extreme fatigue in this case– may be underestimated[13].

An inverse situation occurs in patients undergoing total knee arthroplasty. After regaining the ability to walk following surgery, some patients tend to perceive their preoperative condition as having been much worse than it actually was. The functional success of the treatment leads to a recalibration of their prior state, generating a positive bias in the perception of improvement[14].

These examples illustrate how response shift can alter the interpretation of outcomes in studies that rely on self-reported measures, particularly when follow-up is prolonged and patients undergo processes of physical or emotional adaptation.

Multiple approaches exist to detect this phenomenon. The most commonly used is the *pre-test / post-test / then-test* design, which includes a retrospective assessment of the prior state from the patient's current perspective. In the *then-test*, patients are asked how they felt before treatment, but only after having undergone it for example: *Thinking about it now, how would you say you really were before starting the treatment?*[15]. Comparing the pre-test with the then-test allows detection of recalibration, while comparison between the then-test and the post-test makes it possible to estimate true change according to the patient's current perception[11].

SO, WHAT THEN?

Although both strategic interaction and response shift may initially appear problematic, they actually represent an opportunity. They remind us that patients are not static objects, but individuals who think, adapt, and change. By recognizing these phenomena, we can improve study design, select better measurement tools, and –most importantly– interpret our observations with greater depth.

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