

**A Care Ethics Analysis of the Duke Research Team’s Published Article: “Genomic signatures to guide the use of chemotherapeutics” in the *Nature Medicine* journal**

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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## **Introduction**

In 2007, a research team at Duke University published a paper that introduced an innovative method for using data analytics to examine the human genome and determine which cancer treatment would be most effective for specific patients (Carlson, 2012). After publishing this paper, they initiated clinical trials on 110 patients. When the clinical trials began, the results of the team's research were being investigated and some of its methods had already been proven to be incorrect. Even after being informed of its faulty research, the team continued the clinical trials and refused to retract its paper, claiming that the blatant and dangerous mistakes it made were simply "clerical errors" (Kolata, 2011). After all the trials were finally terminated in 2011, a group of enrolled patients filed a lawsuit against Duke, and in 2015 the lead researcher – Anil Potti – was found guilty of misconduct by the U.S. government and entered into a voluntary settlement where he "neither admitted nor denied findings of research misconduct" (Kaiser, 2015).

This particular case is frequently used as an example of poor scientific practices and the potential pitfalls of using complex software and technology without proper expertise. Although these aspects of the case are very well documented and examined, scholars have provided little to no discussion on the morality of the Duke research team besides to indicate that it did not follow the correct procedures. A large part of this may be due to the nature of scientific research, and the public's corresponding acceptance of a certain amount of risk that human participants are exposed to, especially in medical research. However, failing to investigate and publicize the team's morally inappropriate actions over the entire lifecycle of the study can unintentionally prevent reflection on what it means to be an ethical medical researcher and how to hold this group morally accountable for their actions.

I will examine the case of the Duke research team through a lens of care ethics that I believe will provide a means to illustrate the team's morally unacceptable actions towards a particularly vulnerable group of people – cancer patients. Specifically, I will demonstrate how the team failed to provide proper care by using four sub-elements of care: attentiveness, competence, responsiveness, and responsibility to analyze the team's actions throughout the study and clinical trials.

## **Background**

In 2006, the Duke research team led by principal investigators Anil Potti, MD, and Joseph R. Nevins, PhD published a paper titled “Genomic signatures to guide the use of chemotherapeutics” in the *Nature Medicine* journal (Potti et al., 2006). In the paper, the team claimed to have analyzed data and discovered that treatments for cancer could be personalized for patients based on genomic information in the patient's DNA – specifically genomic signatures of NCI-60 cell lines. Using its results from this study, the team began to recruit for and initiate clinical testing of the treatments on human patients (Carlson, 2012).

After the Duke team's study was published, many other researchers became interested in recreating the study, including two bioinformaticians named Keith Baggerly and Kevin Coombes, who were somewhat skeptical about the results the Duke research team had obtained. Together, they investigated the research and found that there had been multiple, relatively simple mistakes made by the research team during the data analysis process that caused its results to be incorrect. After discovering these errors, Baggerly and Coombes published their findings, but the Duke team ignored their critiques. Only when it became public that the lead researcher – Anil Potti – had lied on his resume about being a Rhodes Scholar, was the article retracted and the clinical trials halted (Kolata, 2011).

## Literature Review

The Duke research team's failure to correctly analyze the data, adequately publish its methods, and respond to critics is well documented and has resulted in multiple research papers detailing the errors that were made throughout the process. These papers have primarily been focused on either dissecting the mistakes made during the research process that caused the team's results to be incorrect, or simply outlining the series of events that occurred before and after the publication of the original study. Although they effectively examine many aspects of the issue, they do not sufficiently address questions about the team's moral obligation to not only the participants in the clinical trials they initiated, but all individuals with cancer who are searching for treatment.

In "Deriving chemosensitivity from cell lines: Forensic bioinformatics and reproducible research in high-throughput biology" – the paper Baggerly and Coombes initially published in response to the Duke research team's study – the two authors provide an in-depth report of the specific problems involved with the Duke research team's study. Their "forensic reconstruction" of the team's data analysis processes found multiple common mistakes. They then go on to explain that while these simple mistakes are relatively easy to fix, "incomplete documentation and lack of reproducibility means that this simplicity is often hidden," causing them to recommend an increased amount of documentation for medical research in the future (Baggerly & Coombes, 2009). While they do thoroughly outline what went wrong during the research and what can be done to improve it, Baggerly and Coombes refrain from delving into the morality of the actions of the team whose research they are investigating.

Bob Carlson, a biotechnology healthcare writer, continues this commentary by providing a higher-level, hindsight aided point of view on the entire timeline of events. He acknowledges

that mistakes in the data analysis were part of the issue, but also questions the original research plan – claiming that “much that went wrong at Duke had to do with the basic principles of science.” He also notes the lack of fundamental research rules enforced during the Duke team’s study, and explains that these “checks and balances” – research institutions, peer-reviewed journals, the IRBs, etc. – are what ensures that the research system functions successfully (Carlson, 2012). Thus, it was multiple failures by numerous individuals and groups that allowed such an event to occur. But although he raises this point, Carlson, just like Baggerly and Coombes, chooses not to investigate the morality of any of the individuals or groups involved, besides from merely noting the things they did wrong.

The current body of research provides an important resource for examining the potential mistakes that can occur during research, but it lacks an analysis of the morality of those involved in the situation. While the relevant scholars seem to agree that there were multiple egregious failures, they do not further address these questionable actions. Using a care ethics framework, I will analyze the actions of the Duke research team to determine morality and provide a judgement on the responsibilities that medical researchers have to the public – and more specifically to those individuals whose lives the research is intended to improve.

### **Conceptual Framework**

The morality of the actions of the Duke research team can be analyzed using a care ethics framework. Initially developed by Carol Gilligan, care ethics is an ethical theory that “emphasizes the importance of relationships.” It branches away from the idea that morals are a product of learning general principles. Instead, it focuses on the development of morals by recognizing how to act in a responsible way towards other people in various contexts. Because all relationships are different and dynamic, the moral way to act is not always the same. By

looking at other perspectives and understanding what other individuals and groups need at different times, moral actions can be tailored in a way that provides the proper level of care (Van de Poel & Royakkers, 2011).

Due to the lack of a uniform set of principles for how to act, care ethics can be a difficult tool to use for a concise moral analysis. One way to break care ethics down into a clearer and more well-defined form is to use Joan Tronto's four sub-elements of care: attentiveness, competence, responsiveness, and responsibility (Sander-Staudt, n.d.).

Tronto defines attentiveness as "a proclivity to become aware of need," competence as "the skill of providing good and successful care," responsiveness as "consideration of the position of others and recognition of the potential for abuse in care," and responsibility as "a willingness to respond and take care of need" (Sander-Staudt, n.d.). In the case of the Duke research team, this would entail:

1. being able to recognize what particular cancer patients need;
2. providing care that improves patients' health conditions;
3. empathizing with cancer patients and therefore taking proper precautions to avoid exploiting them; and
4. being willing to respond and take care of patients.

In what follows, I will examine the nature of the relationship between the Duke research team and cancer patients using a care ethics framework. Specifically, I will use the four previously mentioned attributes – attentiveness, competence, responsiveness, and responsibility – to analyze the research team's actions over the course of the study and clinical trials. Given that

all four of these attributes make up proper care, it is logical then to assume that if an individual or group is lacking even one, then they are acting immorally in a relationship.

## **Analysis**

In their initial research and resulting clinical trials, the Duke research team failed to uphold ethical practices that are standard in medical research. Throughout the process the team demonstrated a lack of proper care for its patients. On their website, the Duke University School of Medicine now boasts an impressive plan for medical research that can “guarantee the responsible management and critical review of scientific data,” but this plan was clearly either nonexistent or unenforced by the university during the research team’s tenure (Duke University School of Medicine, n.d.).

In this particular situation, the researchers were in the role of doctors by providing treatment to their patients. Just as in a normal doctor-patient relationship, the doctor, with their expertise in the field of medicine, has the duty to act in the best interest of their patients, who may not fully understand the field or even their own diagnosis. Through the lens of care ethics, because the research team, as caregivers, had an intimate relationship with its clinical trial patients, they had a duty to provide services that improved their health and wellbeing. The following sections examine each of the sub-elements of care and indicate the actions that illustrate the Duke research team’s failure to both adhere to these principles and act morally.

### *Attentiveness and Competence*

The Duke research team appeared to provide the first sub-element of care – attentiveness – and initially looked poised to provide proper care. However, this trend did not continue, and as the team progressed through the research process, it failed to provide the second sub-element of

care – competence. As mentioned in the conceptual framework, attentiveness means “a proclivity to become aware of need,” and competence means “the skill of providing good and successful care” (Sander-Staudt, n.d.). In the case of the Duke research team, these terms can be defined as being able to recognize what cancer patients need and then providing care that improves their health conditions. This ability to analyze the needs of others and provide effective treatment is especially important in medical research, and specifically cancer research. This is largely due to the time sensitive nature of the disease and the uncertainty around whether or not certain treatments will improve patients’ conditions. According to WebMD, “The earlier cancer is diagnosed and treated, the better the chance of its being cured” (Swiner, 2020), but the American Cancer Society states that there is “no way to know for sure whether treatment will work” (American Cancer Society, 2016). If the treatment they receive is ineffective, or even worse detrimental, it can waste the already small opportunity patients have for treatment and potentially lead to death.

In “Cancer statistics, 2020,” an article for the American Cancer Society, Siegal et al. stated that “cancer is a major public health problem worldwide and is the second leading cause of death in the United States.” Using historical data, the authors predict that there will be over 1.8 million cases of cancer in the U.S. in 2020 and it will cause over 600,000 deaths (Siegal et al., 2020). In most, if not all medical research on cancer, one of the first steps is finding an area where treatment could be improved. By deciding to spend its time investigating how to improve cancer treatment, the team was clearly able to recognize a need within society. Specifically, it chose to research a method for using genomic indicators to guide treatment, whose “promise seemed stunning” (Kolata, 2011). This indicates that the team not only recognized the basic need for improvement, but also appeared to have recognized that the field could benefit from creative,



innovative ideas for treatment. Thus, it can be concluded that the Duke research team did successfully provide attentiveness, the first sub-element of care. This was unfortunately not the case with the second sub-element of care – competence.

One of the main aspects of competence – providing proper care to cancer patients – is to offer treatment that has been proven to be successful or has indicated positive results. A large part of the process of discovering these effective treatments is performing diligent, thorough, and high-quality research, and to have results and methods reviewed by individuals and groups unrelated to the research team. In this case, the Duke research team did neither of those things.

Before the study had even been performed, the team made efforts to remove any “oversight mechanism” that might impede on the publication and testing of its research by others within Duke University. By convincing the university that their research work was particularly unique, members of the team were able to leverage their positions to create a new research division at Duke called the “Institute for Genome Sciences and Policy,” where they were free to operate without significant regulation (Carlson, 2012). This allowed the team to perform and publish a large quantity of research while providing little to no documentation about its methods. Although it was advertising its research as a great success, the lack of relevant published information made it nearly impossible to definitively confirm whether or not its work was truly uncovering innovative new treatments. And while medical research remains a field that cannot exist or improve the lives of the general public without some inherent risk to patients, the team’s conscious and purposeful circumvention of the standard level of supervision rendered its results essentially useless. Thus, because the team chose to ignore proper research protocol, it was already exhibiting incompetence even before the start of the study.

However, the most egregious research errors occurred during the actual performance of the study – specifically during the data analysis process. Two that stand out are an off-by-one error and a labeling error, both of which were discovered by Baggerly and Coombes when they were investigating the results of the study. In the first case, the data for a gene was listed one row above the gene name. In the second, the labels on treatment sensitive and resistant patients were swapped, with treatment sensitive patients being reported as resistant and vice versa. (Baggerly & Coombes, 2009). Thus, during clinical trials, patients might have been accidentally receiving treatment that would have either no effect or possibly a negative effect on them instead of a positive one. These dangerous mistakes would have even been easy to fix if the team had at least documented their methods, but as I previously noted, the team fell short in this aspect as well. This level of negligence and error indicates an obvious lack of competence on the part of the team, because it was unable to provide care that improved patients' conditions.

### *Responsiveness and Responsibility*

As with competence, the Duke research team failed to provide the next two sub-elements of care – responsiveness and responsibility. These two sub-elements especially highlight the team's morally inappropriate actions after the paper had been published and the clinical trials had begun. In this case, responsiveness can be defined as empathizing with cancer patients' and therefore taking proper precautions to avoid exploiting them. Responsibility can be defined as being willing to respond and provide care to the patients. These are particularly important in this case, because cancer patients are an extremely vulnerable population given the lack of treatments available that can effectively cure them or at least prevent the cancer from spreading and worsening their condition.

For examining the team's responsiveness and responsibility, it's useful to discuss its reactions (or lack thereof) to outside questions and criticisms after it initially published the paper. Soon after it was released, many other researchers in the field became interested in recreating the team's innovative method. The two bioinformaticians I mentioned earlier, Keith Baggerly and Kevin Coombes, were some of the most skeptical about it. As they tried to recreate the study, they found that their results were vastly different than those published in the paper. After they reached out to the team to learn about its methods, they became "increasingly convinced that the data didn't add up." To inform the team and warn the public about this, they published their analysis to a medical journal called *Nature Medicine* (Carlson, 2012). If the team had either chosen to take these claims seriously, investigate them, and publicly respond, or had chosen to delay clinical trials, they might have demonstrated some level of responsiveness and responsibility, but instead they ignored Baggerly and Coombes and proceeded to initiate multiple clinical trials on 110 patients based on questionable methodology and research. It would take until 2011, four years after the trials were initiated, before all these trials were halted and discontinued (Carlson, 2012). In the Hippocratic Oath, one of the most historically important texts for medical experts, it commands physicians to state that they will only give treatment that will benefit their patients and "do no harm or injustice to them" (North, 2002). Given the doctor-patient relationship between the research team and the enrolled patients, this oath should have been an important principle that the team used to guide its research. Instead, by both failing to act on glaring errors discovered by multiple other members of the scientific research community, and then failing to take simple precautions to protect its patients, the team failed in its duty of care to its patients, and thus acted morally inappropriately.

Thus far, I have argued that the team's actions indicate that they acted with neither responsiveness or responsibility. Now, some might say that since the team was simply following the normal procedure for publishing and testing new methods for cancer treatment, it cannot be held accountable for both the medical research and Duke University system flaws that allowed the study to make it so far in the research process. To place blame on one team for a larger systematic failure would be illogical. However, the lead researcher Potti and his team members took inappropriate actions in their attempts to provide proof of its methods in order to publish its paper and begin clinical trials. These included "submitting false research data in a grant application, a submitted manuscript, and nine research papers, along with "altering data sets to make drug response predictors look more accurate" (Kaiser, 2015). These actions went initially undetected and allowed the team to fund its research and continue to gain increasing publicity and respect in its field. Members of the team even made an effort to capitalize financially through commercialization of their "innovative" methods via two new companies launched by Duke University (Carlson, 2012). This attempt to monetize the results of the study so soon after its release and without being transparent about its research practices, indicates an obvious and inexcusable lack of responsibility and responsiveness, and thus causes me to stand by my original claim that the Duke research team failed to provide these sub-elements of care in its work.

## **Conclusion**

Using a care ethics framework, I have argued that the Duke research team failed in its moral obligations to the cancer patients that participated in its clinical trials. Shortcomings of the team's original research procedures and their reaction when those research methods and results were called into question had damaging effects that could have been even worse if not for timely

outside intervention from two bioinformaticians – Baggerly and Coombes. Specifically, the team’s failure to provide three of the four sub-elements of care – competence, responsiveness, and responsibility – in its work indicate that it acted immorally towards its patients.

This analysis delved into a well-known, well-documented case of misconduct. While it is one of only a few with such a high level of publicity, it is by no means a rare occurrence. In fact, in 2012 there were 381 journal retraction notices, compared to only 22 in 2001 (Gewin, 2012). That same year, a *British Medical Journal* survey of 2700 scientists and doctors in the UK found that 13% admitted to having knowledge of research misconduct that included “inappropriately adjusting, excluding, altering, or fabricating data” (Tavare, 2012). While in this case the lead researcher, Anil Potti, was technically found guilty of misconduct, he was allowed to enter into a settlement where he did not have to admit guilt for the misconduct. For the sake of all patients receiving research-based treatment, it is important to investigate and publicize misconduct and other morally inappropriate actions so as to promote a greater awareness of these unethical research practices and their consequences within the research community.

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