

Episode: *Author Interview: “How Should We Approach Body Size Diversity in Clinical Trials?”*

Guest: Dania Pagarkar

Host: Tim Hoff

Transcript by: Cheryl Green

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[bright theme music]

TIM HOFF: Welcome to another episode of the Author Interview series from the *American Medical Association Journal of Ethics*. I'm your host, Tim Hoff. This series provides an alternative way to access the interesting and important work being done by Journal contributors each month. Joining me on this episode is Dania Pagarkar, a fourth-year medical student at the University of Southern California Keck School of Medicine in Los Angeles. She's here to discuss her article, coauthored with Drs Erin Harrop and Lisa Erlanger, “*How Should We Approach Body Size Diversity in Clinical Trials?*,” in the July 2023 issue of the Journal, [How We Over Rely on BMI](#). Dania, thank you so much for being on the podcast. [music fades]

DANIA PAGARKAR: Thank you for having me.

HOFF: So, what's the main ethics point that you and your coauthors are making in this article?

PAGARKAR: So, to put it simply, there's a strong argument to be made for the inclusion of higher-weight participants in clinical research and specifically FDA clinical trials. And I think this inclusion can provide robust, more generalizable research and adhere to some of those core principles of medical ethics. We have studies demonstrating reduced effectiveness of vaccines for those categorized as obese, differing responses to chemotherapeutic agents, frequent underdosing of drugs such as antibiotics, and it's clear that further research of body diversity in clinical trials and subgroup analysis of this population is called for. This is not only because of prior legislation such as the NIH Revitalization Act that addresses similar issues for other minorities, but also because as a scientific community, if we have an aim to produce generalizable results, if a certain population's demonstrating differing responses to interventions, then we should be producing research that includes this population and conduct subgroup analysis to understand how this population responds to an intervention.

Unfortunately, we are not yet there in terms of inclusiveness. Even the most recent COVID vaccine trials severely underrepresent and under-analyze a higher-weight population. And it's similarly bleak in the arena of cancer research as well. And so, when we consider those core principles of medical ethics such as beneficence, non-maleficence, and justice, if we want to maximize the benefits of research to society, that includes maximizing benefits to those with higher weight. We should want to avoid harm, such as avoiding inadequately vaccinating a huge chunk of the population that's higher weight. And if we want to adhere to the principle of justice, then larger-bodied patients deserve access to the benefits of research, and active exclusion or a failure to include prevents that.

HOFF: And so, what's the most important thing for health professions students and trainees to take from your article?

PAGARKAR: Yeah. So, I think there's two big points. It's knowing how to structure your research and pick a study population, and knowing how to read published research. So, when

you're forming a study, it's important to ask yourself, are there reasons to include subgroup analysis of higher-weight participants? And some factors you can consider when you're asking yourself this question is, does this target disease have higher prevalence or different mechanisms of action in larger-bodied patients? Is weight stigma impacting the disease course or treatment? Or is the intervention a medication that's delivered intramuscularly? And another thing is when you're looking and reading published articles, it's good to ask yourself, do the participants included in this study represent a wide range of BMIs? Was subgroup analysis done for the higher-weight participants? Are social determinants of health being accounted for? Did those in higher BMIs drop out at higher rates from the study? And if they did, did the study investigate why they were dropping out?

So, I think in general there's a lot of nuance that can be added to both how we look at published research and investigate for inclusiveness of higher-weight participants and also how we engage in future research with that inclusiveness in mind. So, concepts like weight stigma should be paid attention to, and it's important to refrain from suggesting some things such as weight loss as a solution to differing outcomes in a study without concrete data actually backing that claim.

HOFF: And finally, if you could add a point to your article that you didn't have the time or space to fully explore, what would that be?

PAGARKAR: Sure. So, I think while the main focus of this article is to push for legislative and individual efforts to mandate and encourage inclusion of the higher-weight spectrum in research populations, I think it's important to just keep in mind the motivation for doing this. So, differing responses to interventions and differing outcomes for larger-bodied individuals stem from a multifaceted source. So, while there are things like differing pharmacokinetics or altered immune responses at play, things like weight stigma and social determinants of health are important to consider as well.

When I was researching how mandated inclusion of women after the NIH Revitalization Act affected clinical trials, I found that there were notable increases in study population diversity, we had great strides in research, and we discovered a lot of diseases that were more common among women and medications that were more effective for women. And all of this makes the case for inclusion of those with higher weight stronger. But I also found that this inclusion has yet to meet the standards we would hope for. And there's discrepancies that remain between the increased inclusion of women and how they're actually benefiting from this in terms of health outcomes, and cardiovascular health and research is a great example of this. So, in response to these discrepancies, we've seen wide-reaching public health initiatives to educate both patients and health care personnel on addressing biases and misinformation. So, I really think that this inclusion of higher-weight individuals in clinical trials is an important step in that journey towards improved health outcomes for this group. However, like with other minorities, as like with women, as I've explained just now, improving these outcomes is a moving target. It really requires constantly reassessing and trying new things. [theme music returns]

HOFF: Dania, thank you so much for your time on the podcast today and for your and your coauthors' contribution to the Journal this month.

PAGARKAR: Thank you for having me.

HOFF: To read the full article as well as the rest of this month's issue for free, visit our site, journalofethics.org. We'll be back soon with more *Ethics Talk* from the *American Medical Association Journal of Ethics*.