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Correspondence

Avoiding contamination in randomized controlled trial

Sir,

I read with interest the article on improving treatment adherence to antidepressant medication in rural women with major depression, published recently[1]. The authors did a commendable job to compare the effectiveness of enhanced care with usual care in improving treatment seeking and adherence to antidepressant medication in women with depression living in rural India. They have conducted a randomized trial to include six out of 33 villages under a primary health centre (PHC).

The six villages covered by the PHC were randomized into two groups of three villages each namely 'Treatment as usual (TAU)' and 'Treatment intervention (TI)' groups. In TI group, patients were monitored regularly by the community health workers (CHWs), sent to the PHC to consult physician, were given education about depression and its treatment. Further emphasis was put on taking antidepressant medication and they were enquired about possible side effects and their doubts were clarified regarding the same. Also CHWs visited those patients (TI) who discontinued medication and/or those who did not visit the PHC for an initial consultation and encouraged them to resume treatment in the intervention group. In contrast to TI group, patients in TAU group diagnosed with depression were encouraged to seek help from the physician at PHC with no additional input from the CHW.

I have a few concerns regarding the methodology of this study. The authors have included six out of 33 villages based on their proximity to the PHC. Selecting six villages based on proximity makes it prone to contamination. It is likely for the patients (or their families) under TI group to come in contact with the patients of TAU group and disseminate the information shared by the CHWs to the latter. TI group patients or their families can encourage TAU patients on the basis of what CHWs told them regarding treatment compliance with antidepressant medications. People in the control group (TAU) might learn about the importance of taking antidepressant medication and any resultant side effects and adopt it themselves. This may result in treatment cross-over *i.e.* receiving the intervention intended for the other group in a trial. Thus, the flaw called "treatment contamination" is created[2].

The randomization used to select these six villages should have been more rigorous and the six villages randomly picked should have been separated by a reasonable geographical distance which would have avoided contamination. Further the authors could have done intention-to-treat analysis which estimates the effect of recommending a treatment to study participants, not the effect of the treatment on those study participants who actually received it[2]. A study by Sussman *et al*[2] have given CAITT *i.e.* Contamination adjusted intention-to-treat which uses an established statistical technique called instrumental variables (IVs) analysis to adjust for the bias created by contamination.

Kanica Kaushal
Department of Community Medicine
Indira Gandhi Medical College, Shimla 171 001
Himachal Pradesh, India
kanicak8@gmail.com

References

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