Author's response to reviews

Title: Two distinct do-not-resuscitate protocols leaving less to the imagination: an observational study using propensity score matching

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Author's response to reviews: see over
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Dear Editor of BMC Medicine,

We are pleased to re-submit our revised manuscript entitled: “Two distinct do-not-resuscitate protocols leaving less to the imagination: an observational study using propensity score matching”, for consideration as a research article. We thank editors’ and reviewers’ for their comments and suggestions on the prior version of the manuscript.

In this version of the manuscript, we have done a lot of work to revise our manuscript following Reviewer 2’s and the statistical reviewer’s comments and suggestions. We also provided a point-to-point response to each reviewer in the following pages.

This revised manuscript has not been previously published and is not under consideration in the same or substantially similar form in any other journals. To the best of our knowledge, no conflict of interest exists. This study was partly supported by a research grant from Taiwan Ministry of Science and Technology (NSC 101-2511-S-002-007). This study was approved by the Institutional Review Board in MetroHealth Medical Center (IRB07-01218).

Best Regards,

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Dear Dr. Onwuteaka-Philipsen,

Thank you again for your comments on our work. Our response to your comments are as follows:

1. Thank you for reminding us of adding some reflections on the clinical practice for DNRCC patients in the “Discussion” section. We added “DNRCC patients will receive only comfort care after the DNRCC order is in effect, which is similar to the philosophy of palliative care services. To provide comfort care/palliative care to patients admitted to ICU has the potential to enhance the quality of care by alleviating pain, dyspnea, thirst, and shortening the length of stay in ICU while not changing patient mortality and satisfaction. If a patient had a DNRCC order written during an ICU stay, he/she received the following: (1) life-extending aggressive interventions gradually withdrawn; (2) comfort care measures, such as hospice/palliative care consultation, the use of morphine and so on gradually added based on the discussion
between health care professionals and patients/family members; (3) potential transfer of the patient to another non-ICU bed for further care” to the “Discussion” section (highlighted by yellow).

We would like to thank you again for your effort in review of our study. In summary, we are grateful for how your feedback has benefited and advanced our approach to the study. We hope that the current version of this revised manuscript with adding some reflections about palliative care is suitable for publication in this journal.
Dear Dr. Massaro,

Thank you for your comments on our statistics. Our point-to-point responses to your comments are as follows:

<Major Compulsory Revisions>

1. We followed your suggestion to discuss the limitation of using propensity score matching, by adding the following to the third paragraph of the “Strengths and Limitations” subsection: “In addition, the propensity score methodology may also hurt the generalizability of the study results. The objective of this study was to examine the medical care provided to DNRCC, DNRCC-Arrest or Non-DNR patients. For comparing “apples to apples”, we used propensity score methodology to compare the DNRCC-Arrest/DNRCC patients with a subset of Non-DNR patients who were similar in all measurable ways, except for not having a DNRCC-Arrest/DNRCC decision [25, 26]. The subset of Non-DNR patients selected using propensity score methodology was not a good representative of the Non-DNR patients as a whole. Therefore, the study results is
favorable for being generalized to the Non-DNR patients who are similar to DNRCC-Arrest/DNRCC patients, but not to the Non-DNR patient subset who are different from DNRCC-Arrest/DNRCC patients (Table 1).”

2. Thank you for your comment, “The statistical methods that were used to……due to the matching.” However, we believed that comparing the matched pairs on the outcome variables using Student t-test/Chi-squared test is appropriate. Propensity score matching is a good method for simulating randomized controlled trial (RCT). In RCT, the outcomes of the two independent groups, the treatment group and the control group, are examined using Student t-test/Chi-squared test depending on the scale of the outcome variables. Similarly, although the DNRCC-Arrest/DNRCC group and Non-DNR group were matched based on the propensity score, the two groups were still independent of each other, and should follow a similar way of conducting statistics as in RCT. Please let us know if you still have any concerns regarding our answer.

3. In response to your comment, “The authors state that, in Model 1……propensity matching with Mahalanobis’ distance”: Each DNRCC-Arrest/DNRCC patient was matched to a single Non-DNR patient with the nearest propensity score, without providing a propensity score caliper (we did not do one-to-one Mahalanobis metric
matching within a propensity score caliper). One concern of conducting propensity score matching using the nearest propensity score is that, if the sample size of each group is not very different (for example 88 DNRCC patients and 100 Non-DNR patients), the propensity score difference of a matched pair may be significantly large. However, this is not the case in our study. In Model 1, 88 DNRCC patients were matched to 2,051 Non-DNR patients, and in Model 2, 188 DNRCC-Arrest patients were matched to 2,051 Non-DNR patients. Therefore, the propensity score matching in our study may not have the problem of concern we mentioned. Therefore, the propensity score matching in our study may not have the problem of concern we mentioned. To relieve the concern that future readers may have, we added “The mean (±standard deviation) of the propensity score difference of the 88 matched pairs was 0.0497 (±0.1140)” (highlighted by yellow) to the first paragraph of the “DNRCC and Non-DNR Patients” subsection (highlighted by yellow). We also added “The mean (±standard deviation) of the propensity score difference of the 188 matched pairs was 0.0055 (±0.0305)” to the first paragraph of the “DNRCC-Arrest and Non-DNR Patients” subsection (highlighted by yellow).

4. In response to your comment, “a more appropriate and traditional way to…… Please add standardized differences to Table 2”: Thank you for this suggestion. Because we are slightly unclear about your suggestions after reviewing them, we would like to make sure
that our implication about standardized difference is exactly the same as yours in order to accurately follow your suggestions and make revisions. “Standardized difference” is defined as “difference of mean/standard deviation.” If our interpretation is correct, the value which indicates good matching for a variable should be -2~2, not as you pointed out “standardized difference <10%.” We attempted to examine whether it is a good matching for a variable by using “pbalchk” in STATA; the output of statistics showed, “Warning: Significant imbalance exists in the following variables,” when the value is greater than 2 or fewer than -2. In addition, we searched the literature regarding checking propensity score matching using standardized difference, but identified only a few webpages. It would be highly appreciated if you can provide some resources regarding this sophisticated strategy to examine how satisfactory our propensity score matching is.

5. In response to your comment, “As a supportive analysis……in a supplementary appendix”: We conducted sensitivity analysis for DNRCC and Non-DNR, and for DNRCC-Arrest and Non-DNR by building the propensity score models excluding the confounding variable—age. We then checked the associations between the three costs and the DNR decisions using appropriate statistical methods. Please check Supplementary Table 4 and Supplementary Table 6 for the sensitivity analysis for DNRCC and Non-DNR. Please also check Supplementary Table 5 for the sensitivity analysis for DNRCC-Arrest
and Non-DNR. We also added a “Sensitivity Analysis” subsection to the “Methods” section to clearly describe how we did sensitivity analysis (highlighted by yellow on page 11 and page 12). Likewise, we also added a “Sensitivity Analysis” subsection to the “Results” section to clearly describe the results of the sensitivity analyses for DNRCC and Non-DNR, and for DNRCC-Arrest and Non-DNR (highlighted by yellow on page 15 and page 16). All of the sensitivity analyses are shown in Supplementary Table 4, Supplementary Table 5 and Supplementary Table 6.

6. In response to your comments, “Table 1 seems not to contain 40 variables……be included in Table 1, 2, and 4”: Thank you for your suggestion. For clearly demonstrating the comparisons of Elixhauser comorbidity measures between DNRCC and Non-DNR, and between DNRCC-Arrest and Non-DNR before and after the propensity score matching, we provided Supplementary Table 1, Supplementary Table 2, and Supplementary Table 3.

<Minor Essential Revisions>

1. In response to your comments, “Please state why data collection was suspended……”: We added “due to personnel limitations” in the second paragraph of the “Data
2. In response to your comment to “Please present percentages in Table 3”: We added percentages in Table 3 and Table 5 (highlighted by yellow).

3. In response to your comment, “Highly skewed items…… mean and standard deviation)”: We totally agree with your suggestions. However, presenting medians and quartiles is common in studies using nonparametric statistical methods for analysis, not for studies using parametric statistical methods. Because this study used parametric statistical methods such as the Student t-test and propensity score matching for data analysis, it would be of concern if we present data using medians and quartiles, but analyze data using parametric statistical methods. For this reason, please allow us to present the data using means and standard deviations. If you still have concerns, please let us know and we will follow.

We would like to thank you for your effort in statistical review of our study. In summary, we are grateful for how your feedback has benefited and advanced our approach to the study. We look forward to your further comments for Major Compulsory Revisions 4.