Author's response to reviews

Title: Dissemination of the nurse-administered Tobacco Tactics intervention versus usual care in six Trinity community hospitals

Authors:
- Sonia A Duffy (bump@umich.edu)
- David L Ronis (dronis@umich.edu)
- Marita G Titler (mtitler@umich.edu)
- Frederic C Blow (fredblow@umich.edu)
- Neil Jordan (neil-jordan@northwestern.edu)
- Patricia L Thomas (thompatl@trinity-health.org)
- Gay L Landstrom (landstrg@trinity-health.org)
- Lee A Ewing (Lee.Ewing@va.gov)
- Andrea H Waltje (waltjea@umich.edu)

Version: 2 Date: 4 February 2012

Author's response to reviews: see over
Response to Reviewers
Dissemination of the nurse-administered Tobacco Tactics intervention versus usual care in six Trinity community hospitals
MS: 1145788295612145

Thank you kindly for this detailed review. Below, please find our responses to the reviewer’s comments. Our edits have been made in track changes in the manuscript. We look forward to your response.

Major Compulsory Revisions

1. Inclusion criteria: according to the description, any patient who smoked ONE cigarette in the past month would be eligible. Does this include those who did not smoked >100 cigarettes in their lifetime? Given the motivation to quit smoking differ by smoking status (experimenter vs. established smokers), it seems unrealistic to include those who are only experimenting smoking for such an intensive treatment.

Good point and we understand that, from a research point of view, those who have smoked less than 100 cigarettes in a life time are not considered true smokers. However, this is a dissemination study and, from a practice point of view, the Joint Commission standards for treating inpatient smokers (http://www.jointcommission.org/assets/1/6/Tobacco%20Treatment%20Measures%20List1.PDF) does says that ALL patients will be screened for smoking and those that smoke will receive treatment. So yes, all patients will be screened and those who have smoked in the last month will be included.

Having conducted smoking interventions in the inpatient setting, we have never recruited an experimental smoker as these tend to be adolescents, and inpatient smokers tend to be older, long-term smokers with chronic diseases such as heart disease, COPD, and cancer. However, we agree with the reviewer that it is possible that we could run across a young adult experimenter. If this occurs, the intervention is tailored to the individual’s degree of nicotine dependence and ranges from low intensity to high intensity, thus if we were to recruit an experimental smoker, they may only get brief advice to quit without medications.

2. Power analysis: I don’t agree with the authors that this is a quasi-experimental study (since randomization is conducted), and therefore using patient as unit of analysis is not justified. According to the group randomized trial literature, the unit of analysis should be unit of randomization. Simply controlling for clustering of outcome variables by hospital (or hospital unit) does not account for the lack of variation of exposure within an intervention hospital and a comparison hospital.

We understand very well the reviewer’s concern about the statistical design issues as we have discussed these extensively with our Federal Data Safety Monitoring Board (DSMB) and consultants David Murray and University of Michigan statistician Brady West who also raised these concerns. After we explained the purpose of the study and our consideration of other alternative designs and analyses, the DSMB accepted our plan. Understanding the purpose of the study is key to acceptance of our methods.
Since many randomized trials have shown that inpatient smoking cessation works, this phase 4 study was to disseminate and test the effectiveness of disseminating the Tobacco Tactics intervention in real world hospital settings with the goal of sustainability at the end of the study. Implementing the intervention at the facility (hospital) level was the most likely design to remain sustainable once the study was completed. The resources provided by the grant were only sufficient to include 6 hospitals in the study, so 3 will do the intervention and 3 will be controls. Based on our prior study [1], we want the two groups of 3 hospitals to be as equivalent as possible on race mix, number of patients, number of units, and numbers of nurses. Had we randomized the 6 hospitals, it is likely that we would have had an imbalanced group of hospitals.

This is a quasi-experimental, 2 group comparison study testing the effectiveness of the Tobacco Tactics intervention in 3 hospitals compared to 3 hospitals that will not receive the intervention. The hospitals are matched so that the 2 groups will be as equal as possible on race mix, number of patients, number of units, and numbers of nurses. While we could have arbitrarily decided which group of 3 hospitals gets the intervention and which does not, we wanted to reduce investigator bias and flip a coin; there is only 1 flip of the coin that determines that assignment (df-1-1=0). We do not feel that 1 flip of the coin primarily made to reduce investigator bias makes this a randomized trial. Given that we know there are big differences in effectiveness of smoking cessation interventions by hospital unit (e.g., cardiac units has higher cessation rates than other units) we are using hospital units as our unit of clustering in the analyses. See detailed conversation with our DSMB at the end of this review. Note that the coin flip has been changed to a computerized selection, still one electronic coin flip to decide which group of three hospitals gets the intervention and which is the control group.


3. Identification of barriers and facilitators: the section on page 11 seems very vague on how to assess the system level and individual level barriers and facilitators of implementation. What theoretical model of implementation will be used? The authors may need to consult the implementation science literature to better understand the potential barriers and facilitators so that they can measure them in the nurse survey.

The theoretical model used to identify barriers and facilitators to implementation is Social Marketing Theory and we have added more information to the paper on this.
4. Sustainability: the authors provide no information on how to assess potential and actual sustainability of the program after the study. E.g., at the very least, will “ownership” of the intervention by medical staff be measured? Or will they re-contact the master trainers after the study finishes to determine the sustainability of the program?

While we spoke in the procedures section of what we would do to ensure sustainability (e.g., integrate the Tobacco Tactics training into new nurse orientation), the reviewer is correct in that we did not explain our measures of sustainability well and these have been added to the measures section. Basically, sustainability will be measured by comparing whether or not the staff nurses continue to implement the intervention in the post-intervention period, when the research nurses are withdrawn. Some specific measures that we will include are whether or not materials are being used (e.g., Tobacco Tactics manuals), whether the Tobacco Tactics training gets integrated into new nurse training, nurse self-report that they are continuing to implement at 3 month follow up, and patient report of receipt of and satisfaction with the components of the intervention in the post-intervention period.

5. Training timeline: the authors did not mention the time frame for training nurses, and the time frame for intervention implementation and testing.

Our experience is that the time frame for training varies from hospital to hospital based on the degree to which hospitals can release nurses from their work stations to attend training and ranges from 2 to 6 months. This has been added to the paper.

6. Measures: the authors provided very little information on process evaluation of the nurse training and intervention implementation. E.g., do nurses feel the training is useful? Do they know more / are they more confidence about dealing with smokers after receiving the training than before? Also, the authors should measure the components of intervention being implemented as a process measure.

As has been shown by Duffy and others, increased nurses’ confidence in providing cessation services is a huge predictor of actually delivering services and this measure is noted in the paper. Another process measure is that we use is to ask nurses before and 3 months after the training whether or not they do particular aspects of the intervention (e.g., give brief advice or arrange for medication). This measure is an important one and per the reviewer’s request, we have added it to the measures section. At 30-day follow-up, we also ask patients before and after implementation of the intervention whether or not they receive specific aspects of the intervention (e.g., video-tape, medications, etc.) and this is now added to the paper.

7. Nurse survey: to my understanding, the each nurse will only be surveyed once, and will be in rolling fashion. How is this approach going to capture a true representation of barriers and facilitators when some nurses are surveyed shortly after the training and some a few months after?

The reviewer is correct that the procedure for surveying nurses was not clear in the paper. It is now outlined in the paper that each nurse will be surveyed prior to receiving training and again 3 months after receiving training at which time the nurse would have had some opportunity to implement the intervention and provide information about barriers and facilitators to implementation.
8. Intention-to-treat analysis: the authors stated that analysis will be conducted based on the intended treatment not actual treatment received. However, they failed to mention a key feature of intention-to-treat analysis, which is when participants are lost to follow-up, the last follow-up value will be carried forward, so that there will be no missing data. In most cases, this is a conservative approach to because in most of the interventions the outcome variables can only occur once (e.g., diagnosis of a disease). However, in this study, intention-to-treat analysis could result in an overestimation of treatment effect. E.g., someone quits at 6 months but is lost to follow-up at 1 year. According to Intention-to-treat analysis, the individual will be assumed to have stated quit. However, the person could also relapse back to smoking, and if this happen, assuming the individual staying quit would result in overestimation of treatment effect. The authors need to address this issue.

Thank you for pointing out our failure to present this as we agree that imputation should be used so results are available for all subjects in the intent to treat analysis. Carrying forward earlier results (especially on smoking cessation from earlier to later posttests) does bias the results to finding more quitting/cessation at later times than is actually justified. We have now added material adapted from our proposal on our extensive follow up data collection and the use of multiple imputation to fill in missing data.

9. Data analysis: I don’t agree that hospital units (instead of hospital) should be treated as clusters. The “correct” approach will be to use hospital as unit of analysis instead of simply control for clustering, since this approach does not take into account the homogeneity of treatment within a hospital, and use a substantially larger standard error to estimate the treatment effect. Also, unless the authors can be certain that staff in one unit will never talk to staff in another unit about the training and intervention, the interaction between staff of different units violates the independence assumption of statistical approach to be used.

This decision to use hospital unit rather than the hospital as the unit of clustering was made because of the low degrees of freedom and low power of analyses that treat the hospital as the unit of clustering (see discussion with DSMB at the end of this response). This again goes back to the goal of our study of having an intervention implemented at the facility in place so that the intervention can be sustained. If we had the funding to study 20 or more hospitals (which would require a huge amount of funding) we would certainly use the hospital as the unit of clustering, but we simply do not have those resources. As discussed in our reply to the DSMB we will control for the prior level of smoking cessation in the hospital and otherwise attempt to reduce the impact of the hospital on our results. We will also do analyses to determine the effects of the hospitals. The DSMB methodological reviewer accepted our proposed design and analysis—see discussion with DSMB at the end of this response.

10. Cost-effectiveness analysis: I think it is premature to conduct this analysis. Given one of the aims of the study is to determine the barriers and facilitators of program implementation, the intervention cannot be assumed to be implemented in its optimal mode, and therefore the effect would be less than optimal. Using such an effect to conduct cost-effective analysis is likely to lead to underestimation of cost-effectiveness. The authors should focus on determining the best way to implement the intervention to maintain its maximum integrity.
A cost-effectiveness analysis was a requirement for this NIH-funded study. Furthermore, our measures of the intervention’s effectiveness will be lower than would be expected if implementation was optimal, which means our measures of cost-effectiveness will be conservative, and it would be reasonable to expect the intervention to be more cost-effective if implemented optimally. While we will be measuring barriers and facilitators to the intervention, we will also be addressing the barriers as they come up so that implementation can be maximized. In addition, we will be measuring the fidelity of the intervention in a number of ways (asking nurses if they do it, asking patients if they get it, and fidelity checks in a random sample of nurses) so we will have some idea of the degree of implementation. We will use sensitivity analysis to estimate how effectiveness and cost-effectiveness varies based on changes in implementation. We agree with the reviewer that we should focus on determining the best way to implement the intervention to maintain its maximum integrity and we will do that as outlined in the paper.

Minor Essential Revisions

11. How were the six hospital selected into the study? Why weren’t they randomized in pairs but in groups of three? Do all hospitals have emergency services? If not, the types of patients received may differ.

The hospitals were selected from a group of Trinity hospitals in Michigan. To maximize recruitment, we chose the 4 largest hospitals. To represent rural hospitals, we chose the two Muskegon hospitals as they were close together and 1 could be in the intervention group and the other in the control group. Hospitals were not randomized in pairs because doing so might still have given us unequal groups. For example, let’s say we randomized in pairs according to size, we still could have randomized all the hospitals with more minority patients into one group. As it is now, the 3 hospitals together closely match the other 3 hospitals together on #RN positions, # of units, annual discharges, and % minorities. All hospitals have emergency services. If there are baseline differences in the type of patients among the 6 hospitals we can control for these differences by adding these variables as covariates in the analysis. If there are multiple differences and we are underpowered to add all of these variables as covariates, we will create a propensity score to control for these differences.

12. Follow-up: the authors stated on page 10 that smokers how do not return surveys will be contacted. Will the Dillman method be used to increase response rate?

Yes, we use a modified Dillman approach and this is now noted in the paper.

13. Intervention: given the complexity of the intervention, it will be very helpful to have a figure showing the time line of a patient in the study.

Figure 1 has been expanded to show the progression of a patient from first being identified as a smoker to completing the study. Table 1 has been expanded to illustrate the overall study design of the intervention; recruitment of patients (as shown in Figure 1) occurs throughout the entire study.
14. Pharmaceuticals: please provide the details of algorithm used to determine pharmaceuticals stated on page 13.

The pharmaceutical protocol is outlined in Appendix B.

Discretionary Revisions

15. Inclusion criteria: those who are unwilling to complete the questionnaire, unavailable to participate or refuse to participate are not “excluded”. They are non-respondents.

These categories were decided upon by the CHART group as eligibility criteria; thus, we have kept the wording to be consistent with the other CHART studies.

16. Table 1: please expand the table to show the 3 follow-ups.

Table 1 has been expanded to show that follow-ups are included in both the pre- and post-intervention time.

17. Table 2: I would suggest removing hospital names, to protect the study from potential bias.

Names of hospitals have been removed.

DESIGN CONSIDERATIONS COMMUNICATED FROM OUR STUDY TEAM TO THE FEDERAL DSMB ABOUT CONCERNS SIMILAR TO THOSE VOICED BY THIS REVIEWER

The original design proposed was a quasi-experimental design because: 1) many RCTs have already looked at smoking cessation intervention in hospitalized smokers and the challenge remains getting evidence into practice which is best done by teaching providers and implementing at the facility level to enhance sustainability; 2) the RFA called for Effectiveness Research on Smoking Cessation in Hospitalized Patients and stated that quasi-experimental designs were acceptable; and 3) implementing at the facility level is in concert with a recent Institute of Medicine (IOM) report which discusses the need for direct comparison of effective interventions in typical day-to-day clinical care including smoking cessation interventions.

To control for confounding variables we originally proposed a quasi-experimental design dividing the 6 hospitals into 2 matched groups based on hospital size and percentage of minorities (see Table 1 below). To avoid investigator bias in choosing which hospital group is assigned intervention or control, we chose to randomly assign these groups. Because we are randomly assigning, we considered treating this as cluster randomized design in our initial protocol submission to the DSMB, but the DSMB members correctly noted the issues with insufficient df at the cluster level. Noting the concerns of the DSMB, we reviewed the pro’s and con’s of all design options (outlined below), returned to our original quasi-experimental design, but offer some modifications to the statistical plan (also outlined below). The options reviewed and proposed analysis plan follow.
1. We would like to return to the design initially proposed in our grant application which is to **group the 6 hospitals into 2 matched groups** (where the groups rather than the individual hospitals are matched) and randomly assign groups. This would give us \( df = 1 - 1 = 0 \). It seems to us that \( df = 0 \) does not qualify this as a randomized cluster design, but instead makes this a quasi-experimental design which will equalize baseline characteristics among intervention and control sites. If “randomization” is troublesome, we can instead “arbitrarily pick” the intervention and control groups, but this would introduce bias as we already know the more cooperative hospitals. Any other option would detract from our design which facilitates implementation at the facility level. By assigning hospitals rather than patients to conditions, we are really testing the applicability of the intervention in real world hospital settings. So we would like to keep this design if possible.

2. Another possibility is to **match the hospitals into 3 sets of 2 and randomize each pair** which give us \( df = 3 - 1 = 2 \). This is a problem because: a) as noted by the DSMB, \( df = 2 \) is insufficient for a clustered randomized control design, and; b) there is a now a greater possibility of unequal groups on baseline characteristics, particularly racial/ethnic status which we found in our VA studies is a significant moderator of treatment effect. Because of these concerns, we are less comfortable with this design option. However, if the DSMB strongly argues for this modification, we can deal with the unequal groups by controlling for baseline differences in the populations at the 6 hospitals, but will unlikely have the power to include all covariates that differ. If we cannot control for all of the baseline differences between hospitals, we could compute a propensity score to control for these overall baseline differences.

3. To “squeeze more power” we could **randomize all 6 hospitals** (\( df = 6 - 1 = 5 \)), which in our opinion only further exacerbates the concerns about demographic and other potential treatment moderator differences between groups as more hospitals could randomize to one group or another causing imbalance between the groups.

4. To “squeeze even more power”, we could **randomize by hospital units**, but there are several problems with this design. a) There is likely to be substantial cross-contamination, as nurses move across units depending on staffing patterns. b) When the Joint Commission (JC) implements new standards for inpatient tobacco cessation in July 2011, it is possible that control units that “catch wind” of the intervention, begin to implement it to meet JC requirements, which would further the cross-contamination problem. c) We would now be implementing in 6 instead of 3 hospitals which would be beyond the scope of the budget so we have to drop 2 hospitals, decreasing the generalizability of the study as the small rural hospitals will be the ones to get dropped. From a Community Based Participatory Research perspective, after working hard to get these hospitals “on board”, dropping some hospitals is likely to cause hard feelings; to avert this, we would offer those hospitals the intervention, but not do the research there.

5. Similar to the other studies in the consortium, we could **randomize at the patient level** which would maximize statistical power, but introduce new problems. a) We would need to drop from 6 to 2 hospitals and hire intervention nurses as we cannot possibly train all of the staff nurses in the facilities to randomize patients and give it to some patients and not to others as having staff nurses randomize patients would simply be too disruptive to their work flow and even if we could train them, they would more than likely give the intervention to all that need it. b) Dropping from 6 to 2 hospitals further decreases the generalizability of the study. c) Dedicated nurse-delivered interventions have already been tested in RCTs by PI Duffy, the Kaiser Permanente System by the Barr-Taylor group, and many others. d) The patient level RCT greatly reduces the probability that the intervention will be sustainable at the end of the study (which was the goal of the RFA) as dedicated nurses for smoking cessation are not likely to be retained by community hospitals, none of the staff nurses would be trained, and facility level implementation would not be in place at the end of the study.
6. Lastly, we reviewed carefully the papers sent and design suggested by Bill Riley, the CHART project director, to consider a staggered longitudinal design in all hospitals as a design option. This option, however, would require stable month-by-month pre-intervention quit rates. Unfortunately, our experience in the VA is that monthly pre-intervention quit rates are very unstable as they are affected by seasonal variations and historical events. For example heart attacks are more likely to occur in the winter and heart patients often have higher quit rates. Moreover, events like the Great American Smoke-out in November or New Year's resolutions in January can also differentially affect quit rates. So we abandoned this idea.

For the reasons cited above, we asked the DSMB to retain our original quasi-experimental design which was to match the hospitals into two similar groups and give one group the intervention and use the other as a control group. The DSMB accepted our arguments along with some modifications to the data analysis section.

Table 1
Estimated Annual Recruitment

<table>
<thead>
<tr>
<th>Group 1</th>
<th>RN positions</th>
<th># of Units</th>
<th>Annual Discharges</th>
<th>% minorities</th>
<th>Group 2</th>
<th>RN positions</th>
<th># of Units</th>
<th>Annual Discharges</th>
<th>% minorities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital 1</td>
<td>659</td>
<td>11</td>
<td>19,800</td>
<td>70%</td>
<td>Hospital 4</td>
<td>502</td>
<td>12</td>
<td>18,250</td>
<td>31%</td>
</tr>
<tr>
<td>Hospital 2</td>
<td>326</td>
<td>9</td>
<td>17,000</td>
<td>4%</td>
<td>Hospital 5</td>
<td>536</td>
<td>8</td>
<td>20,500</td>
<td>29%</td>
</tr>
<tr>
<td>Hospital 3</td>
<td>765</td>
<td>9</td>
<td>11,400</td>
<td>27%</td>
<td>Hospital 6</td>
<td>765</td>
<td>9</td>
<td>11,400</td>
<td>48%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,750</strong></td>
<td><strong>29</strong></td>
<td><strong>48,200</strong></td>
<td><strong>17,618/48,200 = 37%</strong></td>
<td><strong>Total</strong></td>
<td><strong>1,803</strong></td>
<td><strong>29</strong></td>
<td><strong>50,150</strong></td>
<td><strong>17,075/50,150 = 34%</strong></td>
</tr>
</tbody>
</table>

References