Reviewer's report

Title: Electronic monitoring of non-adherence to medication therapy: examining underlying assumptions

Version: 1 Date: 13 July 2007

Reviewer: Ramani Durvasula

Reviewer's report:

General

---------------------------------------------

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

In the abstract and results section, the authors interpret the finding that an initial increase in non-adherence represented an intervention effect. This is actually in contrast to what might be expected as the classic “Hawthorne Effect” which would suggest that patients would show an initial INCREASE in adherence as a result of being monitored. Theirs is almost a “reverse” intervention effect – with the intervention deleteriously impacting the desired behavior. They may to consider spelling this out further.

In the background section they overstate the utility of MEMS caps stating that they bring about “unprecedented precision” - while they are a great improvement over traditional methods such as self-report – the weaknesses inherent in MEMS caps have long been cited and the authors are urged to pull back from that statement.

The figures and tables the authors use are actually quite useful and do a nice job of organizing the various ways internal and external validity are impacted when using MEMS caps. The authors are also correct in noting that the skewed nature of adherence data requires reliance on non-parametric tests or other non-linear methods, a fact that is often not adequately addressed in the adherence literature.

While this paper is a useful methodological addition to the literature, there are several limitations to this study that the authors should strive to present with greater circumspection.

(1) The period of review was 3 months – a rather long window for retrospective recall. Typically adherence recall deteriorates after 7 days. Issues such as dropping a cap, removing pills etc. could easily have been forgotten, and this deserves mention by the authors.

(2) The collateral report scale is very subjective and poorly operationalized. Additionally, it does not appear to have been subjected to any form of inter-rater reliability analysis – thus what is being called good adherence by one health
provider could be rated by fair as another.

(3) The sample as a whole had VERY high levels of adherence (nearly 96%) – this is unusually high given that most studies of adherence report rates ranging from 50-85%. At the very least, this speaks to the selective nature of this sample. These rates of adherence are not representative and the authors should highlight this fact.

(4) The sample is not well characterized sociodemographically – the authors provide data on age, nationality and gender only. Further data on race/ethnicity, and educational level would have been useful to better understand the sample.

(5) The sample was very selective, and not representative of many of the more heterogeneous samples examined using MEMS caps, particularly HIV+ samples. The need for accurate adherence to highly active antiretroviral therapies used in HIV management made MEMS caps an oft-employed tool in HIV research. However, HIV infected samples in the US are often ethnically diverse, and are often economically disadvantaged. In addition, they often demonstrate much lower rates of adherence. The authors are urged to note the fact that their sample is not representative of the larger population of persons who are post-transplant, and may not reflect the types of samples on whom MEMS caps are employed – as such their findings, while interesting, may not necessarily be replicated in other samples.

The use of MEMS caps can create a false sense of “security” in assumptions about accuracy of measurement – this a potentially useful manuscript for any researchers employing MEMS caps.

---------------------------------------------------------------------

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

This manuscript examines threats to the internal and external validity of adherence assessment using medication event monitoring systems devices such as MEMS caps. The authors highlight 4 assumptions that underlie the internal and external validity of MEMS caps. This is an important methodological issue as studies across a variety of disease models employ MEMS caps. The present authors highlight the fact that while MEMS caps are a significant improvement over traditional adherence measures such as self-report, recognition of some of the potential limitations inherent in using MEMS caps is important.

The study focuses on a relatively select group of patients – patients who are post-kidney transplant and are part of a healthcare system that provides far greater supports than observed in the US. The title of the paper may want to be expanded to clarify exactly what the paper is doing – for example “examining underlying assumptions regarding validity…” (as it is not initially clear what is meant by “underlying assumptions” and possibly acknowledging the type of sample (e.g. in post-transplant patients).

---------------------------------------------------------------------
**Discretionary Revisions** (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests