Reviewer's report

Title: Persistence on prostaglandin ocular hypotensive therapy: an assessment using medication possession and days covered on therapy

Version: 2 Date: 3 November 2009

Reviewer: Alan Robin

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I believe the authors have done a nice job of revising this manuscript. Yet, in the three years since the Wilensky manuscript (19) much has happened to make us realize that tracking glaucoma therapy persistence through pharmacy data base records may not be as valid as it was thought to be. These limitations have not been dealt with by the authors. Problems such as drop execution, electronic documentation of adherence and persistency, and dealing with “how long a bottle of drops should last” are major hurdles that have not been acknowledged in this manuscript. The authors need to both recognize these problems and discuss them at length.

Items 3 and 4: The authors I think may not have understood my comments. There are many ways of assessing adherence and the authors must point out the weaknesses in both this and “days covered to be a “fair” manuscript.

If one looks at the following reference (Am J Ophthalmol 2007;144:533–540) on page 535 the authors will find table 1 (by the way this paper does objectively assess adherence using MEMS devices (electronic tracking) in glaucoma patients. This deals with 4 different measures of adherence. The authors in this current manuscript are basically evaluating percent of doses taken “days covered”. Pharmacy refill data can Not distinguish between someone on a systemic antihypertensive taking a 30 day supply of a q d medication once a day at 8 am promptly and another patient taking two pills at a time so that by the end of two weeks, all of the month’s dose has been taken, leaving no medications for the next two weeks when a prescription can be refilled again. From a pharmacy refill perspective this second patient would have behaved perfectly, but in actuality the patient overdosed for two weeks and under dosed for two weeks.

Objective assessment of eye drop administration (Stone and coworkers Arch Ophthalmol. 2009;127(6):732-736 ) found an average of 1.8 drops hitting the eye. This does not even account for the drops hitting the cheek and floor. Pharmacy data cannot account for coverage, much more important than percent of doses taken. The authors should clearly state this limitation. Might I suggest the authors refer to the following excellent manuscript for a reference addressing this point in subjects with systemic hypertension (BMJ 2008;336;1114-1117 ).

The authors might best consider this in their discussion. Might I add that there are many objective studies of adherence using the Travatan dosing aid also in
the literature. A discussion of the advantages and disadvantages of pharmacy refill data in glaucoma therapy in light of the above references is important.

Point 10: I must disagree. There are many references dealing with drops per bottle and times between refills (the authors have mentioned just a few). However, many patients who are “persistent” and have PBM coverage for their prescriptions will run out before their month is over and not use their own funds to “cover” the time lapse between when their bottle runs out and when they are allowed to refill again. Likewise non-of the studies deal with the number of drops left within a bottle. The authors need to recognize and comment upon this fact in a meaningful way.

Item 15: The authors might and should add that all of these methods do not account for the “human difficulty in applying just a single drop to the eye.” This should be noted.

Item 16: Again the reviewers might add that there are no validated educational methods of instructing subjects.

In the response to Edwards’ comment: The authors should acknowledge that in most prevalence studies approximately 50% of subjects with glaucoma are unrecognized and that in the Baltimore Eye Study, there were 8 times more ocular hypertensives than glaucoma patients. Also, the authors should expand upon their example of “sufficient days supply”.

Edwards 12: As this is a study sponsored by Pfizer, is there a bias in assuming that hyperemia is the cause of early failure? If so, this might be noted.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I am a consultant to both Pfizer, Alcon, and Merck.