

Measuring Persistency and Intraocular Pressure-Controlled Days in Patients Receiving Topical Glaucoma Medications

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Abstract

Investigators have developed methods to estimate the number of healthy days or symptom-free days in randomized trials or population-based settings. Such measures can be used in cost-effectiveness studies or disease management surveillance. This paper suggests that the concept can be extended to measure intraocular pressure (IOP)-controlled days in glaucoma by combining data from randomized trials on IOP control (ie, whether a target IOP or percent reduction in IOP was achieved) with data from pharmacy database studies on drug persistency. Patients with lower rates of persistency would be expected to experience fewer IOP-controlled days as they switch therapies or discontinue topical therapy altogether. Evaluating IOP-controlled days according to patients' topical glaucoma therapies could improve population-based disease management compared with the use of simpler measures that consider IOP measurements at a single point in time.

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Healthy Days, Symptom-Free Days, Disease-Controlled Days

During the 1990s, through its routine household surveillance program, the US Centers for Disease Control and Prevention (CDC) developed a new measure, the number of healthy days, to characterize the nation's health-related quality of life.¹ Telephone interviewers asked respondents to estimate how many days (during the past 30 days) they considered their physical or mental health to be not good; subtracting the not good days from 30 days provides the number of healthy days.² Because all respondents are asked to estimate the number for a retrospective 30-

day period, the mean number of healthy days can be reported. The CDC advocates healthy days as a useful burden of disease measure for population-based surveillance in its Behavioral Risk Factor Surveillance System.¹

Related measures, such as the number of symptom-free days, have been used to evaluate treatments for respiratory conditions, especially when the investigators conducted an incremental cost-effectiveness analysis.³⁻⁵ Methods for estimating the number of healthy days or symptom-free days also can be extended to disease-controlled days more generally. For example, Hood and colleagues⁶ developed an innovative measure of drug treatment effectiveness for patients with diabetes mellitus: symptom-free days with acceptable [glucose] control (SFDAC). These authors used SFDACs in their cost-effectiveness model, which was designed to compare oral drug therapies for diabetes.⁶ To calculate the number of SFDACs, Hood et al used published data from the United Kingdom Prospective Diabetes Study (UKPDS),⁷ a long-term trial that offers a wealth of information concerning the natural history of glucose control and the frequency of adverse effect by type of drug therapy.

The resulting model follows patients with diabetes for 6 months beginning the day first-line monotherapy was initiated.⁶ Patients continued on that therapy unless their glucose was uncontrolled or they experienced an adverse effect, at which point they switched or added therapies. At the end of 6 months, patients were defined

as being on first-line, second-line, or third-line (including insulin) drug therapy. To determine the probability of patients failing first- and second-line drug therapies, the investigators analyzed country-specific pharmacy databases to measure drug persistency. In their example, patients' glucose levels were assumed to be uncontrolled for the first 40 days following therapy initiation, which was referred to as the titration time. Thereafter, patients were considered controlled on days without symptoms, without adverse events, and without elevated fasting plasma glucose values. The rate of SFDACs ranged from 0 per 180 days (0%) for patients who never achieved glucose control to 140 per 180 days (78%) for patients who achieved glucose control with first-line therapy immediately following the 40-day titration period. The number of SFDACs was calculated for various drug treatment strategies.

Intraocular Pressure-Controlled Days

Elevated intraocular pressure (IOP) is a significant risk factor for the development of glaucoma, a group of diseases typified by progressive and irreversible optic nerve damage accompanied by visual field loss.⁸ Direct methods of treating the optic neuropathy of the disease do not currently exist.⁸ However, because reducing IOP levels has been shown to prevent optic nerve damage and to preserve the visual field,⁹⁻¹² IOP reduction is the usual therapeutic target in glaucoma patients and IOP often is used as a surrogate marker of visual function outcome.

Given the importance of IOP as an outcome measure in glaucoma, a composite effectiveness measure conceptually similar to symptom-free days, the IOP-controlled day, can be designed for glaucoma management with topical IOP-reducing therapies. Although it does not make sense to integrate data on symptom frequency for glaucoma because the disease is asymptomatic for most of its natural history, it does make sense to integrate data on IOP control (as reflected by whether a target IOP or percent reduction in IOP was achieved) and on adverse effects.

To model the rate of IOP-controlled days per year for a cost-effectiveness analysis, the method outlined by Hood et al⁶ for calculating SFDACs in diabetes could be adapted. For each first-line therapy, clinical trials could supply the probabilities that patients will achieve IOP control or that adverse effects will occur, while cohort studies of pharmacy claims could provide the probability that patients will fail therapy and switch to or add other IOP-lowering agents. In contrast, conventional measures of IOP control, such as difference in levels of pressure (measured in mm Hg) after 6 or 12 months of therapy capture only a fraction (1/365th) of the natural history that must be taken into account in order to prevent or delay disease progression. By integrating IOP measures collected at several time points during a trial, IOP-controlled days could provide a more comprehensive measure of disease management with less risk of attributing apparent IOP control to random fluctuations on a given day.

Even without developing a formal cost-effectiveness model for IOP-controlled days, persistency studies using pharmacy databases can supplement disease management efforts in managed care settings.¹³ For example, measuring IOP values for all patients on a quarterly basis, the typical visit frequency used in randomized trials, may be impractical in managed care. Moreover, some patients in managed care fail to attend periodic clinic visits at which the level of disease control would be measured. Because patients are more likely to persist with their topical therapy if they achieve their target IOP level and if they experience few adverse effects, patients with lower persistency rates probably experience fewer IOP-controlled days as they switch therapies or discontinue topical therapy altogether. Although data on the IOP-controlled days are not available to validate these assumptions about the value of persistency findings, a reasonable assumption would be that patients cannot achieve IOP control if they obtain an insufficient supply of topical therapy to manage their disease between visits. All other clinical issues

being equal, higher rates of drug persistence should translate into more IOP-controlled days. If measuring patients' IOP control directly, and daily, could be done in such a way that it did not depend on attendance at clinic visits, such a method certainly would be preferable. In the absence of such direct IOP measurements, the value of indirect measures for estimating IOP-controlled days should be considered.

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