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This supplementary material has been provided by the authors to give readers additional information about their work.
eMethods
MANAGEMENT AND OUTCOME OF EARLY AND LATE COMPLICATIONS
All suprachoroidal hemorrhage and endophthalmitis patients were assumed to undergo surgical management with drainage and vitrectomy, respectively, regardless of initial glaucoma surgery. For the purpose of this model, all eyes experiencing either of these adverse events were assumed to result in significant visual loss despite medical intervention.1-4 As such, they incurred the additional cost of management but were later assigned to the ‘blind’ health state.

Surgical success rates after conjunctival advancement for bleb leak5 were calibrated to match the work of Budenz and colleagues, who reported a 92% rate of success in maintaining bleb function. In our model, these patients incurred the additional cost of a second surgical procedure but, based on their preexisting visual field, remained in either the ‘surgical success, moderate visual field’ health state or the ‘surgical success, advanced visual field’ health state. The remaining 8% of eyes both experienced the additional cost of surgical revision and transitioned to a surgical failure health state. Furthermore, eyes of patients with hypotony maculopathy in the trabeculectomy group incurred the cost of surgical correction, which was followed by one of two scenarios. If the visual acuity returned to baseline (90%)6, patients remained in their relative health state, as described above. If the diminished visual acuity persisted (10%), patients moved to a moderate loss of central visual acuity health state.

Revision of the tube shunt using conjunctivoplasty with scleral reinforcement for tube erosion was derived from the work of Low and colleagues who reported a 94% surgical success rate 7. All patients requiring tube revision incurred the additional cost of a second surgical procedure. The surgical successes remained in their assigned visual field/surgical success health state. The remaining 6% transitioned to a surgical failure health state.

The success of penetrating keratoplasty (PK) for corneal edema in trabeculectomy patients were derived from the work of WuDunn and colleagues8 who reported a 45.8% bleb failure after PK, and a 90% survival of the PK in trabeculectomy patients. The success of PKs in tube shunt patients was calibrated to match the work of Alvarenga 9 who reported a PK failure rate of 58%, and a tube failure rate of 26%. All PK patients incurred the additional surgical and medical costs of a PK and were assigned to the glaucoma surgical success or failure states as outlined above. PK failures transitioned to the blind health state.

Diplopia patients incurred the cost of prism (90%)10 or surgical correction (10%).) Diplopia did not affect the rate of progression to surgical failure or risk of visual field progression.

ESTIMATING BASELINE VISUAL FIELD LOSS AND RATES OF PROGRESSION
Assuming a Gaussian distribution, we simulated a sample of 1,000 eyes using the rates of progression (in dB/year) from Folgar et al. (-0.86±0.8)11 and Bhardwaj et al. (-1.01±0.2)12 with a rate of progression of -0.92±0.59 dB/year prior to surgery. As such, 79.2% of eyes progressed faster than -0.60 db/year, or 3dB in 5 years, producing a probability of progression of 0.79 in 5 years. This was converted to an annual probability.
of progression of 0.27, if patients were kept on maximal medical therapy without undergoing surgery, using the equations defined above.

Although IOP reduction was similar between the two surgical procedures in TVT, there are no data suggesting these groups progressed at the same annual rate of glaucomatous visual field loss. As such, we used the progression rates from the work of Folgar, who provided the only peer reviewed study to date comparing rates of visual field change (in dB/year) between eyes that did and did not require adjunctive therapy due to failure. In this study, eyes undergoing filtering surgery progressed at a mean rate of -0.40 ± 0.6 dB/year. As such, 8.25% of eyes progressed greater than -3.00 dB over the five year time horizon. To be conservative, a 10% probability was applied to the surgical success arms of both procedures.

Since there are currently no studies comparing rates of visual field progression (in dB/year) between eyes with successful and failed glaucoma incisional surgeries, visual field data was derived from the work of Folgar and colleagues and cross validated with the visual field data from CIGTS advanced subgroup. We used the scatterplot from Figure 1 of CIGTS to derive a linear regression model that could provide slopes (i.e.: rates of visual field change in dB/year) for the medical controlled and surgical arms in the advanced subgroup (<-10dB) of CIGTS. We obtained the values of -0.18 and -0.12 dB/year in the medically controlled and surgically controlled arms, respectively. This means that eyes controlled on medical therapy progressed on average 1.55 times faster than those undergoing surgery. Likewise, Folgar et al. reported rates of -0.58 ± 1.1 and -0.40 ± 0.6 dB/year in eyes undergoing glaucoma filtering surgery (trabeculectomy and tube) that did and did not require adjunctive therapy due to failure, respectively. This also corresponds to rates approximately 1.50 faster in eyes with failed procedures; we employed the relative rate between the two groups as it is less influenced by differences in rates of progression due to different population characteristics between the two studies.

Given the lack of data from studies with higher level of evidence, rates of progression were varied in the sensitivity analysis.

COSTS

Surgery: Surgical cases were assumed to be one hour in duration for anesthesia billing purposes, with a cost of $197.28. All tube insertions included both codes 66180 and 67255 for scleral reinforcement, with the latter discounted 50% in both CPT and APC for multiple procedures. All surgical procedures, unless otherwise specified, were assumed to include the cost of Vigamox ($114.72) and Pred Forte ($229.29). Each simulated trabeculectomy patient was assumed to incur an additional $100 cost related to extra office visits during the global postoperative period. This cost accounted for lost wages and/or travel costs (3 hours per visit, at $8/hour with an average 4 extra office visits). This assumption was varied in the sensitivity analyses.

Follow up: Follow up costs for both tube and trabeculectomy arms were derived from AAO recommended practice patterns and included two office visits per year at level 92012, one Humphrey visual fields, and one OCT of the optic nerve. Following surgical failure, patients received two additional office visits and one additional visual field test. In addition, $1000 was assigned to individuals suffering unilateral blindness for low vision aids. In this model, postoperative management that occurred during the global period, including bleb needling and suture lysis, was not considered an additional cost.
However, since one-third of trabeculectomy patients\textsuperscript{15} undergo at least one subconjunctival injection of 5-FU, the medication cost was included as a supplemental cost in the trabeculectomy arm. The model also accounted for the cost of healon for AC reformation in 3\% of both surgical arms.

\textbf{Surgical complications:} Costs incurred for any/all complications requiring glaucoma surgery considered the surgeon fee, facility fee, and anesthesia fee related to surgical correction of the adverse event. In addition, post operative medication and any preoperative testing required were incorporated into the surgical costs.

\textbf{SENSITIVITY ANALYSIS}

Variables subjected to one- and two- way sensitivity analyses include early and late failure rates for each surgical intervention, rates of surgical adverse events, rates of progression, time horizon, costs of glaucoma reoperation for surgical failures, cost of increased post-operative visits for trabeculectomy, QALY values, utility associated with surgical failure, decrease in Medicare reimbursement for tube, and costs of supplemental medication.
eResults

SENSITIVITY ANALYSIS

Varying Early and Late Adverse events: Increasing the incidence of visually threatening adverse events to 6% in each surgical arm decreased the absolute reduction in blindness between both surgical arms and the medical arm to 8%. The cost per QALY of trab relative to medication increased to $11,293 and the cost per QALY of tube relative to medication increased to $19,830.

Varying time horizon: Changing the time horizon to 10 years resulted in 11% of trab patients, 10% tube patients, and 36% medically treated patients becoming blind; at 15 years 18% trab, 16% tube, and 50% medically treated patients became blind and at 20 years, 24% trab patients, 22% tube patients, and 57% medically treated patients became blind. At 10 years, the cost of trab over medication was $2570/QALY and tube over medication was $5499/QALY; at 15 years, the cost of trab over medication was $1387/QALY and tube over medication was $3082/QALY and the cost at 20 years of trab over medication was $1235/QALY and tube over medication was $2355/QALY. The relative cost per QALY of tube over medication is listed in table 3.

Varying rates of progression: (see eTable 1) Given the limited data on visual field progression after glaucoma surgery, a two way sensitivity analysis was performed on the rates of progression in the surgical success and failure arms. In all cases, the incremental cost-effectiveness ratios of both surgical procedures over medication was less than $50,000 per QALY. In addition, the cost of tube relative to trab was less than $50,000 and provided marginally better health-related quality of life when compared to trab.

Varying Surgical Failures from MTMT to Reoperation: Since the base case assumed all surgical failures resumed MTMT, a sensitivity analysis was performed to consider the potential cost of reoperation for surgical failure. In the TVT trial, the rate of repeat surgery with tube insertion was 14.3% at 5 years in the trabeculectomy arm and 3.7% in the tube arm. Additionally, 4.7% of tube patients underwent cyclophotocoagulation surgery. Under these circumstances, the cost of tube relative to trab decreased to $18,825/QALY.

Varying travel costs in trab arm, disutility after surgical failure, and cost of medications: Several additional parameters were varied but had no significant impact on costs or utilities of either surgery.

Varying QALY values: When the QALY values were replaced with the QALY regression equations calculated by Rein et. al, the cost of tube over trab increased to $35,947/QALY.

Varying QALY modification for surgical failure: When the additional disutility for surgical failure was eliminated from the model, the cost per QALY of trab over medication decreased to $5735/QALY and tube over medication decreased to $11,735. When the disutility was increased, the cost per QALY of trab over medication increased to $13,166/QALY and tube over medication increased $19,021. When disutility for surgical failure was eliminated, the cost of tube over trab increased to $43,865/QALY. When the disutility was increased, the cost of tube over trab decreased to $17,329/QALY.

Decreasing the Medicare reimbursement for tube surgery by bundling the cost of scleral patch graft: When the surgeon fee and facility fee for scleral patch graft were eliminated from the cost of tube surgery, the cost per QALY of tube over trab decreased to $13,156/QALY.
According to the models describing the relationship between visual field MD and QALY proposed by Rein et al.\textsuperscript{16}, QALY losses accumulate slowly at early stages of the disease and then increase at an accelerating rate once the MD gets worse than -10 dB. Since cost-effectiveness decreases as QALYs gained increase, cost-effectiveness becomes increasingly lower among patients with worse glaucoma. In the TVT, the mean baseline MD was -16 dB and the distribution was skewed towards even worse visual fields – several of whom had poor vision that precluded meaningful automated perimetry - as it is expected in a population undergoing incisional surgery. This means that the increased cost effectiveness ratio we found is likely overestimated (i.e.: more expensive). For instance, based on the Rein et al models and the $2,132 difference we found, for a given patient whose baseline MD was -16 dB the cost-effectiveness ratio would be as low as $16,680; for an MD of -20 dB, the ratio would be approximately $14,213 per QALY gained.

We estimated that the cost of increased visits in the trabeculectomy group from the minimum wage equivalent of the time spent. It is impossible to derive a single value for this cost, as there are many factors at play including geography, employment status, family support, and comorbid illness. For example, an otherwise healthy 60 year old patient living in New York City traveling on the subway will have very different cost burden than a wheelchair bound 85 year old living 20 miles away from their ophthalmologist. To account for this difference, we performed a sensitivity analysis that showed a modest decrease in the ICER as supplemental costs related to number of postoperative visits increased.

It should also be mentioned that there is no consensus on the ideal WTP to use in cost-effectiveness analysis. In fact, it has been argued that using a single WTP for all analysis is not useful\textsuperscript{17}. The WTP depends on many factors including who the payer is and what resources are available; the government, society, and patients often have different priorities when it comes to allocating resources. Likewise, a higher WTP is irrelevant without the necessary funds. Some have hypothesized that WTP should be lower for preventative rather than curative interventions \textsuperscript{18}. Others suggest that analyses in the United States should also include cutoffs of $100,000/QALY and $150,000/QALY\textsuperscript{19}. Despite all of these considerations, the surgeries were well within the conservative and generally accepted WTP threshold of $50,000/QALY.
REFERENCES


12. Bhardwaj N, Niles PI, Greenfield DS, et al. The impact of surgical intraocular pressure reduction on visual function using various criteria to define visual field


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### Table 1. Sensitivity Analysis for Probability of Visual Field Progression in the Markov Model of Surgical Intervention for Primary Open-Angle Glaucoma

<table>
<thead>
<tr>
<th>Prob of VF Progression if Surgical Success</th>
<th>Prob of VF Progression if Surgical Failure</th>
<th>Relative Risk of Progression between Surgical Success and Surgical Failure Groups</th>
<th>ICER between two surgical procedures (S/QALY)</th>
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<td>0.90</td>
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</table>

\(^1\) Base case

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**eTable 2.** Probabilistic Sensitivity Analysis Parameters in Markov Model of Surgical vs Medical Intervention for Primary Open-Angle Glaucoma

<table>
<thead>
<tr>
<th>Variable</th>
<th>Distribution</th>
<th>Tube</th>
<th>Trab</th>
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</thead>
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<td>Early failure</td>
<td>Beta</td>
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<td>0.1 (0.01)</td>
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<tr>
<td>Corneal Edema</td>
<td>Beta</td>
<td>0.017 (0.001)</td>
<td>0.017 (0.001)</td>
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<td>Bleb leak</td>
<td>Beta</td>
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<td>0.02 (.001)</td>
</tr>
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<td>Suprachoroidal hemorrhage</td>
<td>Beta</td>
<td>0.03 (0.001)</td>
<td>0.04 (0.001)</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>Beta</td>
<td>0.01 (0.001)</td>
<td>0.03 (0.008)</td>
</tr>
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<td>Hypotony maculopathy</td>
<td>Beta</td>
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<td>0.03 (0.008)</td>
</tr>
<tr>
<td>Late failure</td>
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<tr>
<td>Visual field progression surgical success</td>
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<td>0.1 (0.01)</td>
<td></td>
</tr>
<tr>
<td>Visual field progression: surgical failure</td>
<td>Beta</td>
<td>0.15 (.03)</td>
<td></td>
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<tr>
<td>Visual field progression: medical therapy</td>
<td>Beta</td>
<td>0.27 (0.05)</td>
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</tr>
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</table>

Data presented as mean (standard deviation).
eFigure 1. Costs and Total Effectiveness Over 5 Years Are Depicted for Trabeculectomy With Mitomycin and Baerveldt Tube Shunt

Cost-Effectiveness Analysis

Tube shunt provides the most costs and most improvement in quality adjusted life years (QALYs). Procedures on the green line are undominated.
eFigure 2. Impact of the Probability of Failure in the First Year for Trabeculectomy and Tube Shunt

Two-way sensitivity analysis varying probability of failure in the first year. Color reflects the surgery that is most cost-effective using a willingness to pay of $50,000/QALY.