Cost-Utility Analysis of Telemedicine and Ophthalmoscopy for Retinopathy of Prematurity Management

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Objective: To evaluate the cost-effectiveness of telemedicine and standard ophthalmoscopy for retinopathy of prematurity (ROP) management.

Methods: Models were developed to represent ROP examination and treatment using telemedicine and standard ophthalmoscopy. Cost-utility analysis was performed using decision analysis, evidence-based outcome data from published literature, and present value modeling. Visual outcome data were converted to patient preference–based time trade-off utility values based on published literature. Costs of disease management were determined based on 2006 Medicare reimbursements. Costs per quality-adjusted life year gained by telemedicine and ophthalmoscopy for ROP management were compared. One-way sensitivity analysis was performed on the following variables: discount rate (0%-7%), incidence of treatment-requiring ROP (1%-20%), sensitivity and specificity of ophthalmoscopic diagnosis (75%-100%), percentage of readable telemedicine images (75%-100%), and sensitivity and specificity of telemedicine diagnosis (75%-100%).

Results: For infants with birth weight less than 1500 g using a 3% discount rate for costs and outcomes, the costs per quality-adjusted life year gained were $3193 with telemedicine and $5617 with standard ophthalmoscopy. Sensitivity analysis resulted in ranges of costs per quality-adjusted life year from $1235 to $18 898 for telemedicine and from $2171 to $27 215 for ophthalmoscopy.

Conclusions: Telemedicine is more cost-effective than standard ophthalmoscopy for ROP management. Both strategies are highly cost-effective compared with other health care interventions.

important gap in knowledge because long-term viability of telemedicine systems will likely depend on economic and cost-benefit tradeoffs.

Cost-utility analysis is a method that quantifies costs against value gained by medical interventions.\textsuperscript{27,28} Utility values are established to represent the patient-perceived quality of life associated with a disease state, ranging from 1.0 (perfect health) to 0.0 (death). These utilities have high construct validity and are stable across sex, ethnicity, education, medical specialty, and presence of comorbidities.\textsuperscript{28} The value resulting from an intervention is expressed in quality-adjusted life years (QALYs), which are defined as improvement in utility multiplied by the duration of benefit.\textsuperscript{29} This article describes a cost-utility analysis comparing telemedicine with standard ophthalmoscopy for ROP management as measured by dollars expended per QALY gained.

### METHODS

#### OVERVIEW

This study was approved by the Columbia University Institutional Review Board. Two ROP management strategies were analyzed from a third-party payer perspective compared with no intervention: (1) standard examinations by an experienced ophthalmologist; and (2) telemedicine examinations by non-ophthalmic personnel using wide-angle imaging devices (RetCam-II; Clarity Medical Systems, Pleasanton, California) with interpretation by a remote ophthalmologist.

Software from TreeAge, Inc (Williamstown, Massachusetts) was used to create decision tree models for each scenario (Figure). Patients enter the tree at the left side and progress along 1 path until reaching a terminal node on the right side. Probabilities at each branch point along with visual outcomes and associated utility values at terminal nodes are based on published literature. Table 1 shows key clinical and economic assumptions.

### PATIENT POPULATION

The CRYO-ROP and Early Treatment for ROP trials provided data regarding visual outcomes, disease incidence, and natural history for patients with BW less than 1251 g.\textsuperscript{1,2,30-32} However, current guidelines state that all infants with BW less than 1500 g or gestational age of 30 weeks or less require examination.\textsuperscript{6} In this study, baseline analysis is performed for infants with BW less than 1251 g and results are extrapolated for infants with BW less than 1500 g.

Among infants with BW less than 1251 g, the CRYO-ROP trial found that 65.8% had ROP, 17.8% had prethreshold disease or worse, and 6.0% had threshold disease.\textsuperscript{31} The Early Treatment for ROP trial determined that 49.3% of prethreshold ROP was type 1.\textsuperscript{32} We define treatment-requiring ROP as threshold

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**Figure.** Decision-analysis tree for retinopathy of prematurity management using telemedicine and standard ophthalmoscopy. Published literature is used to assign outcome probabilities at each branch point and to determine visual outcome utility values at the right side of the terminal nodes (triangles). The bottom 2 legs follow a path identical to that of the “Referral” leg above (+).

### Table 1. Key Clinical and Economic Assumptions for Cost-Utility Analysis of Retinopathy of Prematurity Management Using Telemedicine and Standard Ophthalmoscopy

<table>
<thead>
<tr>
<th>Assumption</th>
<th>Details</th>
</tr>
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<tbody>
<tr>
<td>Infants require an average of 5 examinations to determine whether treatment-requiring ROP develops.</td>
<td></td>
</tr>
<tr>
<td>A telemedicine system would refer all cases of type 2 prethreshold disease or worse to an experienced ophthalmologist for examination.</td>
<td></td>
</tr>
<tr>
<td>Infants found to have treatment-requiring ROP receive 1 session of laser photocoagulation to the affected eye(s), and visual outcomes are modeled based on results from published literature.</td>
<td></td>
</tr>
<tr>
<td>Sensitivity and specificity of telemedicine and standard ophthalmoscopy for detection of treatment-requiring ROP are imperfect and are modeled based on results from published literature.</td>
<td></td>
</tr>
<tr>
<td>Telemedicine imaging by trained, nonophthalmic staff produces photographs of acceptable quality for bilateral interpretation in 95% of patients.</td>
<td></td>
</tr>
<tr>
<td>Visual acuity in the study population remains stable throughout life, and all patients have an average life expectancy of 77.5 y.</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: ROP, retinopathy of prematurity.
or type 1 disease, which represents 11.9% (where 6.0% + [0.493 (17.8% − 6.0%)]) of infants with BW less than 1251 g.

Premature infants are typically examined every 1 to 2 weeks until diagnosis of either full vascularization or treatment-requiring ROP. This study assumes that all infants receive a total of 5 examinations and that infants with telemedicine who develop type 2 ROP or worse receive 3 telemedicine examinations before referral, followed by 2 ophthalmoscopic examinations.

ACCURACY OF TELEMEDICINE AND OPHTHALMOSCOPIC EXAMINATIONS

A practical telemedicine strategy would likely require image capture by trained neonatal personnel using a commercially available camera. One study showed that 6% of photographs captured using the RetCam were unreadable on initial imaging, and another showed that 95.4% of patients had acceptable images captured within the first 2 attempts. Therefore, this study assumes that readable images are captured in 95% of patients and that infants with unreadable images are referred for standard ophthalmoscopy.

In our telemedicine model, all patients believed by remote experts to have type 2 ROP or worse are referred for ophthalmoscopy and further appropriate management. We have previously shown that the mean sensitivity and specificity for detection of treatment-requiring ROP, when remote graders believe that images represent type 2 ROP or worse, are 0.933 and 0.902, respectively. Based on an 11.9% incidence of treatment-requiring ROP among patients with BW less than 1251 g, the positive predictive value among these referrals (ie, the fraction of patients referred for type 2 ROP or worse who truly have treatment-requiring ROP) was calculated by Bayes’ theorem to be 0.361. Similarly, the negative predictive value (ie, the fraction of patients not referred who truly do not have treatment-requiring ROP) was calculated to be 0.990.

Although ophthalmoscopic examination is a standard technique, we have shown that there is significant variability in accuracy and agreement, even among recognized experts, for identifying treatment-requiring ROP. Following previously used methods, this study assigns sensitivity and specificity for ophthalmoscopic diagnosis of treatment-requiring ROP equal to those of diagnosis by image interpretation (0.867 and 0.962, respectively).

VISUAL OUTCOMES AND UTILITY SCORES

Four possible outcomes were defined (Table 2): (1) correctly treated (infant with treatment-requiring ROP received laser photocoagulation), which were assigned visual outcomes based on the study by Ng et al that reported results 10 years after laser photocoagulation; (2) correctly untreated (infant without treatment-requiring ROP did not receive laser photocoagulation), which were assigned outcomes based on a natural history CRYO-ROP patient cohort with 5.5 years’ follow-up; (3) incorrectly treated (infant without treatment-requiring ROP received laser photocoagulation), which were assigned the same visual acuity outcomes as the correctly untreated group based on the assumption that laser photocoagulation for non–treatment-requiring ROP neither improves nor worsens visual outcome on average; and (4) incorrectly untreated (infant with treatment-requiring ROP did not receive laser photocoagulation), which were assigned outcomes based on the CRYO-ROP untreated control group with 15 years’ follow-up.

Visual outcomes in the better-seeing eye were used for analysis based on findings from the CRYO-ROP study that 82.5% of infants with threshold ROP have bilateral disease. For the remaining 17.5% of infants with unilateral threshold disease, visual outcome in the untreated eye was assigned a value equal to that of the correctly untreated group described earlier.

Snellen visual acuities were converted to decimal visual acuities, which were then converted to utilities based on a published formula: utility = 0.374x + 0.514, where x is the decimal visual acuity. For example, a Snellen visual acuity of 20/20 would have a decimal visual acuity of 0.4 and a utility of 0.664, and a Snellen visual acuity of 20/200 would have a decimal visual acuity of 0.1 and a utility of 0.551. Based on published guidelines, visual acuities reported as counting fingers, fix and follow, or centered, steady, maintained were assigned a decimal visual acuity of 0.025 (utility, 0.523); visual acuities reported as hand motions or unsteady, unmaintained were assigned a decimal visual acuity of 0.0125 (utility, 0.519); and visual acuities of no light perception were assigned a decimal visual acuity of 0 (utility, 0.514).

ADJUSTMENTS FOR INFANTS WITH BW LESS THAN 1500 g

Adjustment for the population of infants with BW less than 1500 g required the following. First, ROP incidence was adjusted using BW data from the Vermont Oxford Network, a worldwide collaboration of more than 600 neonatal intensive care units. From the Vermont Oxford Network registry, the ratio of infants with BW less than 1500 g to those with BW less than 1251 g is 1.46. Because the percentage of infants with BW between 1251 and 1500 g who develop treatment-requiring ROP is extremely low, we calculated an approximately 8.1% (or 11.9%/1.46) incidence of treatment-requiring ROP among infants with BW less than 1500 g. Second, positive and negative predictive values of telemedicine and ophthalmoscopy were recalculated using this 8.1% incidence. Third, visual outcomes for the natural history cohort were adjusted with Vermont Oxford Network data, which show that 86% of infants with BW between 1251 and 1500 g have no ROP.

COSTS

Medicare reimbursements from 2006 were used because this is the most standard system for representing medical costs in

Table 2. Weighted Visual Acuity Outcome Levels and Associated Utility Values Used to Calculate Cost-Effectiveness of Telemedicine and Standard Ophthalmoscopic Retinopathy of Prematurity Examinations

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Visual Acuity</th>
<th>Utility Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correctly treated</td>
<td>20/39</td>
<td>0.704</td>
</tr>
<tr>
<td>Correctly untreated</td>
<td>20/32</td>
<td>0.748</td>
</tr>
<tr>
<td>Incorrectly treated</td>
<td>20/32</td>
<td>0.748</td>
</tr>
<tr>
<td>Incorrectly untreated</td>
<td>20/67</td>
<td>0.626</td>
</tr>
</tbody>
</table>

a Correctly treated means that an infant with treatment-requiring retinopathy of prematurity received laser photocoagulation. Correctly untreated means that an infant without treatment-requiring retinopathy of prematurity did not receive laser photocoagulation. Incorrectly treated means that an infant without treatment-requiring retinopathy of prematurity received laser photocoagulation. Incorrectly untreated means that an infant with treatment-requiring retinopathy of prematurity did not receive laser photocoagulation. Data are obtained from published literature and are shown in this table for a population of infants with birth weight less than 1500 g.

b Data are from the article by Ng et al.

c Data are from the article by Ng et al.

d Data are from the article by Ng et al.

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the United States. Costs were determined by multiplying the 2006 conversion factor (37.8975) by the relative value unit of particular Current Procedural Terminology (CPT) codes. Specific costs were modeled (Table 3). First, ophthalmoscopy was represented as an inpatient consultation (CPT-99254) for initial examinations, as subsequent hospital care (CPT-99223) for follow-up examinations, and with extended ophthalmoscopy (CPT-92225/92226) for half of all examinations. Second, management of treatment-requiring ROP was represented as laser photocoagulation (CPT-67228), which was modeled as bilateral for 82.5% of patients and unilateral for 17.5%. It was assumed that no additional hospitalization costs were associated with ROP care and that no costs would accrue after initial treatment because laser codes have a 3-month postoperative period. Third, telemedicine examinations were represented as technical and professional fees for fundus photography (CPT-92250).48-50

COST-UTILITY AND PRESENT VALUE ANALYSIS

Based on the probabilities and visual outcomes described earlier, the expected utility value of each strategy was determined. Costs per QALY gained from telemedicine and ophthalmoscopy compared with no intervention were determined. This benefit was applied over the lifetime of patients assuming that average life expectancy is 77.5 years and is unaffected by having treatment-requiring ROP. It is well established in health care economic analysis that future outcomes must be discounted because the implied value of future health benefits is lower than current health benefits. In this study, all of the ROP management costs are modeled to occur in the present and all of the QALY outcomes are discounted at a 3% rate based on recommendations from the Panel on Cost-effectiveness in Health and Medicine.49-50

SENSITIVITY ANALYSIS

Sensitivity analysis was used to determine the effect of changes in the baseline values described earlier on the cost-effectiveness of each strategy. This was performed for discount rate (0%-7%), incidence of treatment-requiring ROP (1%-20%), sensitivity and specificity for ophthalmoscopic detection of treatment-requiring ROP (75%-100%), percentage of readable telemedicine images (75%-100%), and sensitivity and specificity for remote detection of treatment-requiring ROP based on referral at a cutoff of type 2 disease or worse (75%-100%).

One-way sensitivity analysis was performed for the population of infants with BW less than 1500 g. When changes in one variable inevitably affected values of other variables (eg, changes in sensitivity and specificity must affect positive and negative predictive values, changes in ROP incidence must affect outcome utility values), this was incorporated into the analysis.

RESULTS

Among infants with BW less than 1500 g, the discounted lifetime costs per QALY gained by telemedicine and ophthalmoscopy were $4870/0.1525 ($3193/QALY) and $6460/0.1150 ($5617/QALY), respectively. Among infants with BW less than 1251 g, the discounted lifetime costs per QALY gained by telemedicine and ophthalmoscopy were $5590/0.1992 ($2807/QALY) and $7030/0.1594 ($4410/QALY), respectively (Table 4).

For infants with BW less than 1500 g, 1-way adjustments in parameter values resulted in costs per QALY gained from $1235 to $18 989 for telemedicine and from $2171 to $27 215 for ophthalmoscopy (Table 5). The telemedicine strategy was more cost-effective than ophthalmoscopy across all of the lower and upper limits of variables tested.

COMMENT

Our key finding is that telemedicine is more cost-effective than standard ophthalmoscopy for ROP management. This is the first study to our knowledge that has compared the cost-effectiveness of these 2 strategies from a third-party insurer perspective.

As early as the 1950s, telemedicine pilot programs have been implemented using support from government agencies. Although these projects demonstrated clinical and technical feasibility of telemedicine, virtually all were terminated after their initial funding period because they were not economically self-sustaining. In the United States, Medicare reimburses predominantly for real-time telemedicine encounters in rural areas, and many payers reimburse for store-and-forward interpretations in specialties such as radiology. Not surprisingly, successful existing telemedicine programs have been established in locations where it is economically advanta-
geistous, such as military and prison settings. Given the shortcomings of current ROP management strategies,7-10 telemedicine may represent an alternative approach that third-party payers will consider reimbursing because of its demonstrated cost-effectiveness.

Cost-utility analysis incorporates medical outcomes using evidence-based data and patient-perceived value. Because utility values transcend demographic characteristics and allow for direct comparison across different medical specialties, this method has been proposed as a strategy for allocation of health care resources.27,28 Javitt et al52 reported that the cost-effectiveness of standard ophthalmoscopy and cryotherapy for ROP care was $2488/QALY in 1988 dollars depending on the exact examination strategy. Brown et al39 found that the cost of laser treatment and cryotherapy for threshold ROP, without considering costs of ophthalmoscopic examination, was $678/QALY gained in 1998 dollars. Our study models both ROP examination and treatment using laser photocoagulation, incorporates results from recent guidelines and outcome studies, and is consistent with these earlier findings. It is also useful to compare with studies regarding cost-utility of other medical interventions. Within ophthalmology, laser treatment of threshold ROP has been shown to be among the most cost-effective interventions ($678/QALY), whereas anterior chamber paracentesis with carbon dioxide and oxygen therapy for central retinal artery occlusion is among the least ($6.5 million/QALY).46 Within general medicine, cost-utilities have found to be $6880/QALY for coronary bypass graft surgery for left artery main disease and $327 500/QALY for liver transplant.47 It is proposed that $100 000/QALY gained should represent a cost-effective intervention39 and that $50 000/QALY gained should represent a highly cost-effective intervention.28,34,53 Using these criteria, both telemedicine ($3193/QALY) and standard ophthalmoscopy ($5617/QALY) for ROP management would be considered highly cost-effective (Table 4).

An important component of this study is that numerical values are assigned to represent accuracy of ROP examinations. The underlying scientific background warrants explanation. Sensitivity and specificity of telemedical ROP diagnosis have been thoroughly characterized against ophthalmoscopy as an assumed reference standard,12-21 and the most detailed of those results are applied to the current study.12,14 We previously studied agreement and accuracy of plus disease diagnosis by a group of 22 recognized ROP experts and found k to be 0.19 to 0.66, sensitivity 30.8% to 100%, and specificity 57.1% to 100%.54,55 Finally, we have shown that agreement between telemedical and ophthalmoscopic ROP examinations is extremely high when images are captured by a trained neonatal nurse, that neither modality has a systematic tendency to overdiagnose or underdiagnose ROP, and that telemedicine may actually be more accurate in some cases.20,21 These findings support the notion that neither telemedicine nor ophthalmoscopy has perfect accuracy. For these reasons and because studies designed to measure accuracy of ophthalmoscopy by multiple examiners would likely be impractical owing to infant safety concerns,20 we believe it is most reasonable to assume that the accuracy of ophthalmoscopy is equal to that of image-based ROP examination.24 We emphasize that our sensitivity analysis (Table 5) demonstrates that telemedicine continues to have greater cost-effectiveness than ophthalmoscopy across a range of parameter values, including wide variations in diagnostic accuracy of both telemedicine and ophthalmoscopy. This advantage persists in a population of infants with BW less than 1251 g (data not shown). Taken together, these results demonstrate that our cost-utility findings are highly robust.

This analysis is performed from the third-party insurer perspective, meaning that only direct medical costs and outcomes are considered. Although it excludes a number of societal costs and benefits, this third-party perspective is widely used throughout the ophthalmic literature because there is no consensus about which societal factors to include.27,28,38,46 In a telemedicine strategy, benefits to ophthalmologists might include decreased travel, opportunity cost savings, and qualitative matters such as satisfaction. Images could also be used for secondary purposes such as teaching, research, and improved clinical care through comparison with prior photographs. These factors are not relevant to direct medical spending be-

Table 5. One-Way Sensitivity Analysis of Cost-Effectiveness of Telemedicine and Standard Ophthalmoscopy for Retinopathy of Prematurity Management Among All Infants With Birth Weight Less Than 1500 g

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Value</th>
<th>Low Value</th>
<th>High Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of readable images</td>
<td>95 (3193/5617)</td>
<td>75 (3707/5617)</td>
<td>100 (3076/5617)</td>
</tr>
<tr>
<td>Discount rate for utility</td>
<td>3 (3193/5617)</td>
<td>0 (1235/2171)</td>
<td>7 (6733/11 842)</td>
</tr>
<tr>
<td>Incidence of disease</td>
<td>8.1 (3193/5617)</td>
<td>1 (18 898/27 215)</td>
<td>20 (2548/3711)</td>
</tr>
<tr>
<td>Specificity of telemedicine</td>
<td>90.2 (3193/5617)</td>
<td>75 (2835/4305)</td>
<td>100 (4070/7959)</td>
</tr>
<tr>
<td>Sensitivity of telemedicine</td>
<td>93.3 (3193/5617)</td>
<td>75 (5175/5617)</td>
<td>100 (3531/5617)</td>
</tr>
<tr>
<td>Specificity of ophthalmoscopy</td>
<td>96.2 (3193/5617)</td>
<td>75 (2345/7703)</td>
<td>100 (3361/4246)</td>
</tr>
<tr>
<td>Sensitivity of ophthalmoscopy</td>
<td>86.7 (3193/5617)</td>
<td>75 (2835/4305)</td>
<td>100 (4070/7959)</td>
</tr>
<tr>
<td>Incidence of disease</td>
<td>8.1 (3193/5617)</td>
<td>1 (18 898/27 215)</td>
<td>20 (2548/3711)</td>
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<td>0 (1235/2171)</td>
<td>7 (6733/11 842)</td>
</tr>
</tbody>
</table>

Abbreviation: QALY, quality-adjusted life year.

*References 2, 6, 12-14, 20, 21, 30-32, 36, 37.

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cause they are not generally reimbursed, and they are therefore excluded from our analysis. However, we note that they may favor telemedicine. Also, study costs were derived from Medicare reimbursement values because this standardized payment system is a reasonable proxy for costs and allows for comparison with most studies in the ophthalmic literature.\textsuperscript{27,28} We emphasize that this is the accepted method for performing health care cost-effectiveness analysis\textsuperscript{27-29,38,45,46} but acknowledge that these Medicare charges may not capture the true cost of ROP management. For example, some physicians negotiate retainer fees from hospitals in addition to receiving third-party payments for ophthalmoscopic examinations. If this factor were considered, it might further favor the telemedicine strategy. Moreover, the costs of telemedicine imaging devices and the salaries of personnel operating them are excluded from this analysis. In standard cost-utility analysis, it is assumed that these latter costs are recovered through technical fees associated with procedures. Finally, in cost-utility analysis, the ramifications of infants incorrectly untreated by telemedicine or ophthalmoscopy are considered to be fully represented by the decreased utility outcome in that group (Table 2). Specifically, this study is not intended to quantify the financial effect of medicolegal liability, and it is not necessarily clear which strategy would be more affected in these situations. In a telemedicine strategy, the availability of photographic documentation could protect physicians from liability or could increase medicolegal risk by subjecting images to heavy scrutiny. A related study examined the cost-effectiveness of photographic ROP screening in the United Kingdom from a societal perspective, with mixed results depending on the approach used.\textsuperscript{23} Further studies may elucidate the cost-benefit effect of these societal factors.

Several additional limitations should be noted. Ocular and systemic complications of ROP treatment were not modeled. It was felt that these complications are infrequent and that they would be unlikely to affect infants with telemedicine and those with ophthalmoscopy differently. In the current ROP care paradigm, infants are frequently transferred between hospitals to receive second-opinion ophthalmoscopic examinations or to undergo laser photocoagulation. These costs are not included in the study and would likely favor telemedicine. Previous studies involving cataract surgery and age-related macular degeneration have examined the cost-benefit effect of treating the first eye compared with the second eye.\textsuperscript{57,58} We chose to model management of all of the affected eyes because we feel that the risks of infancy-acquired blindness are too great to consider intentionally excluding examination or treatment of 1 eye.\textsuperscript{32} This study was not designed to examine workflow engineering issues related to real-world telemedicine systems, such as turnaround time of image interpretation or interstate medical licensure.\textsuperscript{59} These must be understood before the widespread adoption of telemedicine to ensure that patient care is not compromised.

Overall, this study shows that telemedicine is more cost-effective than standard ophthalmoscopy for ROP management. If workflow, reliability, medicolegal, reimbursement, and acceptability issues can be addressed, then telemedicine may become a useful strategy for improving ROP care while decreasing costs.

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Author Contributions: Dr Chiang had full access to all of the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

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