The Cost of Juvenile-Onset Recurrent Respiratory Papillomatosis

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Objective: To assess the medical costs and the number of quality-adjusted life years lost owing to juvenile-onset recurrent respiratory papillomatosis (JORRP).

Design: We examined hospital and physician charges for JORRP surgical procedures in Maryland in 1994 adjusting for inflation and the cost-charge ratio. Centers for Disease Control and Prevention data on treatment intensity for JORRP were augmented with a review of treatment records for 18 patients with JORRP. Sensitivity analyses were performed. To illustrate the application of our cost estimates, we compare the costs of JORRP to the costs of the surgical procedures that would be necessary to prevent it.

Results: We find that the present value at birth of the cost of a single case of JORRP is $201,724 (range, $61,822-$474,334). The annual cost for a single case of JORRP is $57,996 (range, $32,407-$94,114). The annual cost of JORRP in the United States is between $40 million and $123 million depending on the prevalence. Cesarean section (CS) for women with condyloma has been suggested as a potential strategy to prevent JORRP, but its efficacy remains to be determined. Our results suggest that if only 1% of the CSs actually prevented JORRP, this strategy would be a cost-effective means to prevent JORRP.

Conclusions: Studies to reduce the uncertainty surrounding the efficacy of CS and the effect of both CS and JORRP on families need to precede consideration of a policy of CS for women with clinically evident genital condyloma. Patients should be kept thoroughly informed about the role of CS for the prevention of JORRP and the nature of the remaining uncertainties.


Juvenile-onset recurrent respiratory papillomatosis (JORRP) is a condition with an incidence rate of 0.4 to 1.2 cases per 100,000 person-years that affects roughly 254 to 763 US children each year. Children with JORRP must undergo repeated costly treatments to reduce the size of recurrent warty lesions in the upper airway. The disease places a heavy burden on families who are often ill-equipped to cope with it.

Despite technical developments in the therapy of JORRP, scientific understanding that would help to prevent it remains limited. Some preventive interventions of unproven efficacy are being considered including vaccination against human papillomavirus or performing prophylactic cesarean sections (CSs) for women with clinically evident genital condyloma. To date, there are no estimates of the cost of JORRP to the US health care system that would suggest whether investments in research and prevention of this disease are potentially cost-effective.
METHODS

The present value of the total benefits derived from a prevented case of JORRP is calculated in dollar costs and quality-adjusted life-years (QALYs). The assumptions behind these estimates of cost and disease burden are varied to assess sensitivity of the results. These estimates are subsequently compared with the additional costs of a policy to perform elective CS for all pregnant women who enter the ninth month of pregnancy having genital condyloma visible on physical examination. This study adheres to published guidelines for conducting cost-effectiveness studies. We adopt the perspective of the medical sector.

MEDICAL BENEFIT

The medical benefit of preventing JORRP can be expressed in prevented medical costs. Most of the medical costs of JORRP are incurred as children undergo repeated laser surgical procedures to ablate laryngeal lesions. Most children undergo fewer than 15 procedures in a lifetime, but some undergo far more, and a handful of children are unfortunate enough to require tracheostomy. Most children begin their surgical experience after the age of 2 years and continue to have operations for many years.

NUMBER OF SURGICAL PROCEDURES

The National Registry for Recurrent Respiratory Papillomatosis has enrolled 399 children with JORRP (defined as active cases younger than 18 years) from 20 different tertiary care centers across the United States. Because the national registry provides a cross-sectional view of prevalent cases from infancy to late adolescence, the reported annual mean number of surgical procedures of 4.4 (range, 0.03-18.9) is likely to be weighted downward by the presence of less intense cases from the older age groups.

From a clinical standpoint there is wide variation in the duration of JORRP; an individual case is characterized by alternating periods of exacerbation and latency. The type of long-term prospective data on disease intensity required to adequately model the dynamic nature of this disease do not exist. As an alternative, we assume that, on a population basis, the disease follows a simple process: incident cases flow into a pool of prevalence that after an average dwell time releases a flow of remissions back to a state of health. In equilibrium the incidence rate equals the remission rate. To a first approximation the remission rate equals the number of prevalent cases divided by the dwell time. Applying these approximations to the Centers for Disease Control and Prevention estimates of US prevalence (1400-2226 cases) and incidence (254-763 cases per year) leads to the estimate that average population dwell time in the diseased state is 2.9 to 5.5 years or an average of 4.2 years. The notion of “population dwell time” will have little relation—to the observed duration of disease in any individual patient—particularly because of the prolonged relapsing nature of any individual case. As an approximation, the population perspective is appropriate only for policy analysis—it should not be used for prognosis in clinical practice. We believe that if anything, 4.2 years understates the true duration with which the population of patients with JORRP endures a disease intensity of 4.4 surgical procedures per year.

MEDICAL COSTS PER SURGERY

Treatment costs for patients with JORRP are incurred primarily at each operation, although physicians provide nonsurgical services such as monitoring disease progression and providing medical therapies for the disease. Based on a review of the practice style of a single surgeon and 217 patient encounters for JORRP, we found a ratio of 1 surgical encounter for every 3 nonsurgical visits.

The cost of each nonsurgical visit is estimated as the fee from the Maryland Resource-Based Relative Value Scale (RBRVS) fee schedule for an office visit for an established patient. Providing medical therapies for the disease. Based on a review of the practice style of a single surgeon and 217 patient encounters for JORRP, we found a ratio of 1 surgical encounter for every 3 nonsurgical visits.

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The calendar year 1997 costs for the practice of a single surgeon and 217 patient encounters for JORRP are based on the Maryland Health Services Cost Review Commission hospital charges for visits to hospitals by patients younger than 20 years who had as their diagnosis benign neoplasm of the larynx. The Health Services Cost Review Commission collects administrative data for every hospitalization in the state of Maryland. Hospital costs in

multaneously setting all of the parameters at their extreme values. The Figure presents a “tornado diagram” to display the sensitivity of the estimates to perturbations of individual parameters. The diagram indicates that the estimates are the most sensitive to changes in the discount rate and surgical procedures per year. A similar exercise with the parameters used for QALYs suggested that the case-fatality rate was the most crucial parameter making up the estimates of QALYs.

COMMENT

We have estimated that the lifetime disease burden of an average patient with JORRP can be expressed as 2.01 QALYs. The lifetime costs to the medical sector alone are in the range of $201,724. To illustrate how these estimates can be applied to policy analysis one can consider what medical costs of CS could be justified by the medical costs of JORRP. Evidence that JORRP is less common in children born by CS has motivated some to consider a policy of offering CS to women with clinically evident genital condyloma. The efficacy of such a policy remains unknown.

Of the 4 million women giving birth each year in the United States, approximately 3.1 million have vaginal deliveries. Of these, approximately 1% are thought to have clinically evident condyloma. What if a policy calling for CSs in the 31,000 pregnant women with condyloma offered a disease preventing benefit to
The average charge from 47 randomly selected patients with a diagnosis of JORRP was $4400 in 1994, which when inflated to 1997 dollars and subjected to the Maryland-cost charge ratio leads to the cost estimate of $4374 in 1997 dollars. Thus each surgery is associated with hospital costs of $4374 + physician costs of $339 + 3 outpatient visits at 3 × $38 (or $104) for a total cost of $4817 per surgery.

The National Registry for Recurrent Respiratory Papillomatosis reports that 11% of 397 children have ever had a tracheostomy.7 However, Derkay et al found a lifetime prevalence of tracheostomy of 14% of children described in a survey of practicing otolaryngologists. Tracheostomy remains a last resort in the treatment of JORRP. To our knowledge, there are no published studies of the medical costs incurred by patients who underwent tracheostomy for JORRP. Medical costs for patients with conditions requiring tracheostomy for mechanical ventilation assistance suggests that these costs exceed $100,000 per year.9 Patients with JORRP generally do not require mechanical ventilation assistance so their costs could be lower. Uncertainty about tracheostomy maintenance costs incurred by patients with JORRP is modeled by using a range of figures (mean range) from $75,000 ± $15,000 per year. We assume that these costs are incurred over a 4.2-year time horizon for 14% of the population with JORRP.

QUALITY OF LIFE AND COSTS PER DISEASE EXACERBATION AND SURGERY

Based on Johnson et al10 the Quality of Well-Being (QWB) score of adults for 1 day of severe shortness of breath was 0.68 (reference range, 0–1). Assuming that adult QWB can be scaled similarly to children and that each operation is associated with 14 days of severe shortness of breath leads to the estimate of 0.0012 lost QALYs per surgical procedure.

DEATH

With the provision of regular and timely medical intervention, death is a rare complication of JORRP. The Centers for Disease Control and Prevention’s death certificate database11 lists 64 deaths in patients aged between 0 and 24 years from benign and malignant neoplasms of the larynx (International Classification of Diseases, Ninth Revision codes 937.1 and 161.2 for 1979-1995. This corresponds to about 4 deaths per year. Misdating and underreporting of deaths in a vital events registry is a well-known phenomenon that may lead to underestimates of the true value. However, there are likely to be rare pediatric laryngeal neoplasms besides JORRP mixed in with the Centers for Disease Control and Prevention’s database making this an erroneous overestimate. Anecdotally, in the last 12 months there have been 4 deaths of patients with JORRP among the nearly 200 self-referred children and youth whose families are members of the Recurrent Respiratory Papillomatosis Foundation a national nonprofit organization (W. Stern, PhD, e-mail communication, August 10, 1999).

The relevant mortality rate for our consideration would need to be expressed as a case-fatality rate of deaths per incident of JORRP. Using as a denominator, the estimated total US prevalence of 254 to 763 cases per year, the estimated 4 deaths per year correspond to a case fatality rate of 324 per 100,000 to 1,372 per 100,000 or roughly 1000 per 100,000.

Preventing the US burden of new incidences of JORRP would save roughly 4 statistical lives of children per year. We assume these deaths occur at a mean age of 8.8 years which is the average age of patients in the national registry.6 Quality-adjusted life-years are calculated as follows:

QALYs Lost in 1 Year of JORRP =

\[\frac{(\text{Days Ill})/365)}{3} \times (QWB \text{ Score}) + (\text{CFR}) \times PV(75−8.8),\]

where CFR represents the case-fatality rate and PV stands for present value operator using a 3% discount rate at baseline.

Lifetime QALYs are computed as the present value of a stream of the annual QALYs computed above for a duration of 4.2 years in the baseline analysis. The analysis assumes an arbitrary maximum lifetime of 75 years. The stream of costs begins at the average age of onset of the disease. Armstrong et al1 report a mean age of onset of JORRP of 3.8 years in the National Registry for Juvenile-Onset Recurrent Respiratory Papillomatosis. In the absence of JORRP, there is no guarantee that each of those saved lives would offer QALY scores of 1 for every year until age 75 years. Few people attain optimal health over a full lifetime. Mathematically the process of assuming less than optimal health in these future life years is identical to applying higher discount rates to future life years. We thus assess the sensitivity of our QALY estimates to discount rates as high as 10%. We use a discount rate of 3% for our baseline estimate.
ment to a clinician who combines emerging evidence and judgment in an attempt to prevent a high-cost pediatric disease.

**CONCLUSIONS**

The potential for there to be as much as $123 million in annual medical cost savings from preventing JORRP is a strong justification for public investment in research that will help lead to its prevention. A prospective study of the efficacy of preventive interventions would be one of the more costly research tasks in this area, but would be justified by the costs of the disease.

Substantial uncertainty remains to be resolved before policymakers will be in a position to recommend CS as a nationwide policy for all pregnant women with visible genital condyloma. In the interim, parents at risk ought to be given the opportunity to weigh the existing evidence in a context that appropriately conveys the remaining and substantial uncertainty about the potential benefit of CS. A clinician whose best judgment supports the recommendation of

variables, range, and sources for juvenile-onset recurrent respiratory papillomatosis (JORRP)*

<table>
<thead>
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<th>Variable</th>
<th>Baseline</th>
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*Md HSCRC indicates Maryland Health Services Cost Review Commission; HCFA, Health Care Financing Administration; and CDC, Centers for Disease Control and Prevention.

Tornado diagram showing the results of the sensitivity analysis. The solid vertical line represents the cost estimate of $201,724 per case of juvenile-onset recurrent respiratory papillomatosis; horizontal bars, the range of cost estimates obtained by setting each variable at the lower and upper limit of its range and holding all other variables constant at their baseline value; and top bar, the range obtained by simultaneously setting all variables at the limit of their range.

Discount Rate (0.10-0.00) | $133,190 - $243,586
No. of Surgical Procedures per Year (3.5-5.3) | $161,379 - $242,068
Statistical Disease Duration (3.4-5.0 y) | $163,357 - $239,149
Tracheostomy Cost ($60,000-$90,000) | $176,472 - $227,975
Prevalence of Tracheostomy (9%-13%) | $176,472 - $227,975
Hospital Cost ($3500-$5249) | $188,336 - $213,748
Physician Cost ($354-$532) | $200,368 - $203,080
No. of Office Visits Between Surgical Procedures (2.4-3.6) | $201,375 - $202,973
Cost per Office Visit ($30-$46) | $201,724

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prophylactic CS to prevent JORRP could be practicing cost-conscious medicine.

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REFERENCES


18. de Zulueta P. Elective caesarean section on request: patients do not have right to impose their wishes at all cost [letter]. BMJ. 1999;318:120.

19. MacKenzie IZ. Should women who elect to have caesarean sections pay for them [letter]? BMJ. 1999;318:1070.
REFERENCES


Correction

Calculation Error. In the article titled “The Cost of Juvenile-Onset Recurrent Respiratory Papillomatosis,” by Bishai et al, published in the August 2000 issue of the *Archives* (2000;126[8]:935-939), an error in the spreadsheet used to calculate the costs of juvenile onset respiratory papillomatosis (JORRP) produced an incorrect estimate of cost and discounted quality-adjusted life-years (QALYs) in the “Results” subsection of the “Abstract” and the first 2 paragraphs of the “Results” section on page 935. The corrected paragraphs should read as follows:

“Annual costs incurred by a statistical case of JORRP are estimated to be $29,946. Setting all parameters at their extreme values, the range for this estimate is $19,101 to $43,267. The present value of the lifetime costs are estimated at $104,159 in the baseline estimate with extreme values of $43,267 to $218,067. Based on the estimated prevalence, the annual medical costs of JORRP in the United States are estimated at $42 to $67 million.

We estimate the burden of lost QALYs at 0.31 per year of disease. Setting all parameters at their extreme values, the range for this estimate is 0.10 to 0.96 QALYs lost per year of JORRP. The estimated number of discounted lifetime QALYs lost due to a single case of JORRP is 1.21 with an extreme range of 0.26 to 4.89 QALYs.”

We gratefully acknowledge Harrell Chesson, PhD, in calling these errors to our attention.