

Utility Outcome Measures for the Treatment of Ameloblastomas during Childhood

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Background: Our objective was to determine the potential impact of the surgical treatment of ameloblastoma in children through validated health state utility outcome measures.

Methods: A survey-based preference health utility assessment using the visual analog scale, time trade-off, and standard gamble methods was undertaken among a general population sample. Quality-adjusted life years were derived from these measures. A one-way ANOVA was used for statistical analysis, with a mean (*P*) value of 0.05 considered significant. Demographic parameters were individually assessed as possible predictors of each utility score.

Results: In total, 86 participants took part in this study, with a mean age of 29.9 years. Greater utility scores were observed among participants reporting no religious beliefs ($P = 0.025$, $t = 2.28$). No other demographic parameters showed statistically significant prediction of utility score. From the mean utility scores (\pm SD) (visual analog scale = 0.60 ± 0.17 ; time trade-off = 0.65 ± 0.22 ; standard gamble = 0.64 ± 0.20), a gain of 30.0, 32.3, and 32.1 quality-adjusted life years may be derived, respectively. All utility outcome measures suggested that an ameloblastoma during childhood is perceived as more burdensome than several debilitating conditions, such as cleft lip and palate.

Conclusions: To attain perfect health, participants would theoretically undergo surgical treatment of an ameloblastoma during childhood, with willingness to trade off 28.2 years of life and accepting a 35.7% risk of death. The objective assessment of the perceived burden of an ameloblastoma affliction during childhood may inspire cost-utility or cost-effectiveness analyses at broader societal levels. (*Plast Reconstr Surg Glob Open* 2020;8:e3311; doi: [10.1097/GOX.0000000000003311](https://doi.org/10.1097/GOX.0000000000003311); Published online 22 January 2020.)

INTRODUCTION

Ameloblastoma is the most common odontogenic tumor, despite a low annual incidence of 0.5 cases per million.¹ The most frequently afflicted individuals are adults between the ages of 40 and 50 years, but diagnosis spans a wide age range of 8–92 years and represents 25% of jaw tumors in children.^{1,2} It typically presents with asymptomatic swelling, most commonly in the mandible, followed by the same in the maxilla.³ Its growth is slow and typically

benign, but has potential for local invasion of maxillofacial structures.¹ If untreated, its growth may lead to complications ranging in severity from tooth loosening to facial deformity and, ultimately, fatality.¹ Radical surgical management is the current mainstay of treatment for aggressive and invasive subtypes.^{3,4} Postoperative morbidity can be significant, especially in the pediatric population with ongoing bone growth. Literature on ameloblastoma in the pediatric population is currently scarce.

Based on clinical and radiographic presentation, ameloblastomas are typically considered in 4 subtypes, with the conventional solid/multicystic type being the most common and most aggressive.^{1,4} Less common subtypes include the unicystic, peripheral, and malignant ameloblastomas.¹ The former is considered special due to its tendency to affect younger patients, predilection for maxillary invasion, morphological characteristics, and its response to conservative treatment.⁵ This may include enucleation alone, or combined with marsupialization or other adjunctive measures, followed by long-term

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radiographic monitoring.^{5,6} Surgical enucleation is exemplified in Figures 1 and 2.

Although there is evidence of a benefit of adjuvant radiation or chemotherapy on malignant subtypes or on those deemed inadequate surgical candidates, the possibility of future personalized therapies is highlighted by recent findings of common BRAF and Sonic Hedgehog pathway mutations, along with sensitivity to the respective pharmacological inhibitors.^{3,4}

Radical surgical management, resection with wide margins of adjacent uninvolved tissue, is the current mainstay of treatment for the more aggressive subtypes, to mitigate the possibility of persistence or recurrence.^{3,4,6} With subsequent reconstructive procedures often being required, this approach is not without morbidity, especially in the pediatric population with ongoing maxillofacial growth.⁶

The health burden of living with ameloblastoma from a young age must be counter-balanced with the risks and complications inherent to undergoing an extensive surgical resection. In a decision-making model of resource allocation for healthcare policy, utility outcome measures are quantifiable values with many uses.⁷ Utility scores can be obtained from 3 different questionnaires, the visual analog scale (VAS), the time trade-off (TTO), and the standard gamble (SG), and can be utilized to calculate quality-adjusted life years (QALYs)—a valuable measure of years lived in perfect health in health economics.⁸

Therefore, the aim of this study was to determine the health utility outcome measures and QALYs gained by the surgical treatment of pediatric ameloblastomas. The hypothesis is that these will be comparable with values previously reported for head and neck neoplasms.

METHODS

This study was conducted according to our institution's research ethics board requirements and in accordance with the declaration of Helsinki. An online survey was distributed to healthy adult volunteers, from April 2018 to May 2020. Participants were recruited from an advertisement placed on a university forum, without any monetary incentives for participation. The first part of the survey collected demographic data, including age, sex, religious beliefs, ethnicity, level of education, employment status, and income. In the second part, participants were shown a photograph of a 10-year-old child with a

voluminous ameloblastoma of the lower jaw. A description was provided, mentioning the benignity of these tumors, with an extremely low risk of malignancy and without any decrease in life expectancy. However, they were instructed that ameloblastomas can slowly grow into significant deformities of the jaw, potentially leading to functional, psychological, and aesthetic limitations.

Respondents were asked to complete the 3 aforementioned utility assessment questionnaires for the surgical treatment of an ameloblastoma, all while attempting to imagine themselves as being the pictured patient. In the VAS, participants were asked to rate their general health state, given the scenario by choosing a number from 0 (representing death) to 100 (representing perfect health). The utility measure of the VAS was calculated using the following formula⁹:

$$\text{Utility} = \text{reported health state score} \div 100$$

The TTO assessment required participants to choose whether they would undergo a surgical resection while “trading off” a given number of years of life expectancy to live in perfect health, or to continue living in the health state, as described in the scenario. Participants were instructed that their life expectancy would be of 80 years, and the number of years that they wished to trade off was determined by going back and forth from 1 to 80 until a point of indifference. The utility measure of the TTO was calculated using the following formula⁹:

$$\text{Utility} = \frac{(\text{number of years lived with ameloblastoma} - \text{number of years traded off at the point of indifference})}{\text{number of years lived with ameloblastoma}}$$

For example, if estimating that living 50 years in perfect health (death at 60 years) is equivalent to living 80 years with the ameloblastoma (death at 90 years), the utility measure would be calculated by subtracting the time traded off from the time living in that health state divided by the life expectancy $((80 - 30)/80 = 0.625)$.

In the SG questionnaire, participants were instructed to “gamble” with the choice of living in the described health state for 80 years, or undergoing resection with X% probability of living in perfect health, but with 1 - X% chance of death. The X number was calculated until both preferences were equivalent, indicating the point of



Fig. 1. Pediatric ameloblastoma. (A) Pre-operative image of an ameloblastoma of the right mandible. (B) Post-enucleation image of the right mandible showing the tumor cavity.

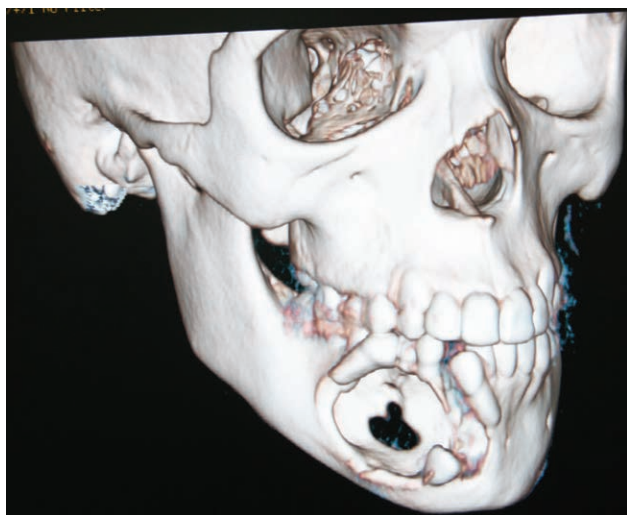


Fig. 2. 3D scan image of a right mandibular defect post-enucleation.

indifference. The utility measure of the SG was calculated using the following formula⁹:

$$\text{Utility} = \frac{(1 - \text{risk of death at point of indifference})}{100}$$

For example, if living in this current health state for 80 years is considered equivalent to taking 80% chance of health but 20% chance of sudden death, then the SG utility would be $80/100 = 0.80$.

From these utility measures, the QALYs associated with the procedure can be calculated using the following formula, with a life expectancy of 50 years, as standardized in the literature¹⁰:

$$\text{QALY} = \text{utility score} \times \text{number of years of life expectancy.}$$

For example, if the TTO utility were 0.60, the QALYs would be equal to that value multiplied by 50 years of life expectancy, corresponding to 30 QALYs.

SPSS, version 24 (IBM, Chicago, Ill.) was used to perform the statistical analysis. Participant demographics are presented as measures of central tendency, namely means and interquartile ranges. Utility measures are presented as means with SDs. These were analyzed with a one-way ANOVA for independent measures to determine whether there was any significant difference among the 3 questionnaires, with a *P* value of 0.05 considered significant. Furthermore, participant demographic variables were tested against the utility measures in a multivariable analysis to determine if there were any confounding factors.

RESULTS

In total, 86 participants agreed to partake in this study. **Table 1** shows their demographic characteristics. The mean reported age was 29.9 ± 10.9 years. A greater proportion of participants were identified as women (60%) when compared with men (39%). A majority reported some religious beliefs (54%). There were 66% respondents identifying as White, as opposed to 17% identifying as Asian and 8% as Arab. Most participants reported an

Table 1. Participant Demographic Characteristics

Characteristic	N
Age	29.9 ± 10.9
Gender	
Men	32 (39)
Women	53 (60)
Would rather not say	1 (1)
Religion	
Christianity	33 (36)
Islam	4 (5)
Judaism	9 (11)
No religious beliefs	38 (46)
Other	2 (2)
Ethnicity	
African American/Black	1 (1)
Arab	7 (8)
Asian	15 (17)
White	57 (66)
Latin American	3 (4)
First Nations, Inuit, or Metis	1 (1)
Other	2 (2)
Education	
High school diploma (DES)	2 (1)
CEGEP diploma	19 (23)
Undergraduate degree	40 (46)
Graduate degree	25 (30)
Employment	
Full-time	29 (33)
Part-time	5 (6)
Unemployed, not seeking employment	2 (2)
Retired	1 (1)
On disability leave, unable to work	1 (1)
Student	48 (57)
Annual household income	
<\$10,000	3 (6)
\$10,000–\$19,999	4 (6)
\$20,000–\$29,999	3 (6)
\$30,000–\$39,999	1 (2)
\$40,000–\$49,999	4 (8)
\$50,000–\$59,999	6 (12)
\$60,000–\$69,999	8 (13)
>\$70,000	25 (44)
Would rather not say	32 (39)

Data are presented as mean ± SD or numbers, with percentages in parentheses.

Table 2. Summary of Utility Scores for Ameloblastoma

Utility Score	Mean ± SD	QALYs
VAS	0.60 ± 0.17	30.0
TTO	0.65 ± 0.22	32.3
SG	0.64 ± 0.20	32.1

educational achievement, including or beyond a collegial diploma, 46% at an undergraduate level, and 30% at a postgraduate level. The majority were students (57%), followed by full-time employed (33%) and part-time-employed (6%). Annual household income was reportedly >\$70,000 among 44% of participants, as opposed to <\$30,000 in 18% (**Table 1**).

The mean VAS utility score was 0.60 ± 0.17 , which may be translated to a mean of 30.0 QALYs (**Tables 2** and **3**). The scores ranged from 0.2 (worst health state rating) to 0.95 (best health state rating). On the TTO, respondents scored a mean of 0.65 ± 0.22 . In other words, they were willing to trade off 28.2 years of life expectancy to regain a perfect state of health through a wide surgical resection of an ameloblastoma during childhood. This represents a mean of 32.4 QALYs (**Table 3**). Finally, the SG yielded a mean utility score of 0.64 ± 0.20 , indicating willingness to gamble a 36% chance of death to recuperate a perfect

Table 3. Comparison of Utility Scores for Ameloblastoma and Other Conditions

Condition (reference)		Utility Scores		
		VAS	TTO	SG
Ameloblastoma		0.60 ± 0.17	0.65 ± 0.22	0.64 ± 0.20
	QALYs	30	32.3	32.1
Unilateral facial paralysis ¹¹		0.56 ± 0.18	0.76 ± 0.22	0.79 ± 0.21
	QALYs	28	38	39.5
Severe facial disfigurement requiring facial transplant ¹²		0.46 ± 0.02	0.68 ± 0.03	0.66 ± 0.03
	QALYs	23	34	33
Monocular blindness ¹²		0.60 ± 0.28	0.82 ± 0.16	0.87 ± 0.14
	QALYs	30	41	43.5
Binocular blindness ¹²		0.34 ± 0.18	0.62 ± 0.27	0.60 ± 0.28
	QALYs	17	31	30
Cleft lip and palate ¹³		0.69 ± 0.18	0.85 ± 0.16	0.84 ± 0.18
	QALYs	34.5	42.5	42
Primary surgery for head and neck cancer ¹⁴		0.76 ± 0.20	0.95 ± 0.13	0.93 ± 0.17
Salvage surgery for head and neck cancer ¹⁴		0.48 ± 0.13	0.98 ± 0.04	0.98 ± 0.04
Total laryngectomy ¹⁵		n/a	0.57 ± 0.06	n/a
Oropharyngeal cancer and transoral robotic surgery ¹⁶		0.67 ± 0.06	n/a	0.95 ± 0.01
Locoregional laryngeal head and neck cancer ¹⁷		n/a	n/a	0.62
Non-laryngeal head and neck cancer ¹⁷		n/a	n/a	0.61

Data are presented as mean ± SD or numbers.
QALY, Quality-Adjusted Life Year.

state of health that lasts 80 years. Translated into QALYs, this represents a mean of 32.1 (Table 3).

Variability of utility values according to participant demographics is reported in Table 4. Mean VAS, TTO, and SG were 0.593, 0.632, and 0.653 respectively among respondents identified as women, as opposed to 0.599, 0.643, and 0.618 respectively among respondents identified as men, which was not found to be statistically significant. Amongst those reporting religious beliefs, utility scores were slightly lower on all 3 questionnaires, namely 0.560 for the VAS, 0.648 for the TTO, and 0.607 for the SG. Only the VAS score was significantly different ($P = 0.025$, $t = 2.277$) when compared with respondents reporting no religious beliefs (VAS = 0.645). According to educational background of participants, utility scores did not differ significantly. When compared with those

employed, utility scores were greater among participants reporting being students, with a VAS, TTO, and SG of 0.597, 0.649, and 0.652, respectively. However, this failed to reach statistical significance. Finally, there were no significant differences among participants of different household income brackets.

DISCUSSION

Ameloblastoma is the most common odontogenic tumor and represents a quarter of jaw tumors in childhood, a time during which functional and esthetic implications are further complicated by skeletal immaturity.^{1,2} Using health-related utility scores, this study showcases the similarity between the perceived burden of an ameloblastoma during childhood and various other debilitating conditions.

Table 4. Utility Scores as a Variable of Demographic Factors

	VAS	TTO	SG
Gender			
Women	0.593 ± 0.184	0.632 ± 0.233	0.653 ± 0.190
Men	0.599 ± 0.162	0.643 ± 0.208	0.618 ± 0.223
<i>P</i>	0.881	0.985	0.454
Religion			
Religious beliefs	0.560 ± 0.184	0.648 ± 0.207	0.607 ± 0.182
No religious beliefs	0.645 ± 0.158	0.648 ± 0.227	0.686 ± 0.221
<i>P</i>	0.025	0.997	0.075
	$t = 2.277$		
Education			
Less than undergraduate degree	0.610 ± 0.187	0.676 ± 0.163	0.691 ± 0.179
Undergraduate degree	0.591 ± 0.191	0.616 ± 0.244	0.601 ± 0.216
Graduate degree	0.602 ± 0.148	0.676 ± 0.206	0.670 ± 0.195
<i>P</i>	0.918	0.442	0.195
Employment			
Student	0.597 ± 0.17	0.649 ± 0.225	0.652 ± 0.222
Employed	0.586 ± 0.182	0.631 ± 0.199	0.619 ± 0.173
Other	0.85 ± 0.071	0.906 ± 0.133	0.825 ± 0.106
<i>P</i>	0.121	0.214	0.343
Household income			
<\$10,000–\$29,999	0.465 ± 0.176	0.538 ± 0.305	0.575 ± 0.302
\$30,000–\$59,999	0.582 ± 0.131	0.602 ± 0.181	0.605 ± 0.175
>\$60,000	0.613 ± 0.173	0.671 ± 0.230	0.681 ± 0.209
Would rather not say	0.632 ± 0.181	0.674 ± 0.171	0.638 ± 0.168
<i>P</i>	0.065	0.269	0.446

Data are presented as mean ± SD, unless otherwise indicated.

Considering the limited resources available in most healthcare economies, informed decisions simultaneously based on medical outcomes and on the value of the care provided are paramount. Economic studies can help elucidate an appropriate course of action for clinicians faced with selecting the most beneficial intervention in proportion to cost. Cost-utility analysis (CUA) features a preference-based assessment of one's state of health. Utility measurement consists of eliciting participants' relative preferences for given health states, along with their functional and esthetic implications.⁹ The VAS, SG, and TTO are validated utility measures essential to CUA.⁹ In a single numerical value, the QALY derived from utility score assessment adds the additional layer of quality of life associated with a given life expectancy, thereby helping better interpret the value of being in the described health state.^{10,18} The QALY can either be used as an independent point of comparison among various procedures, or to value the outcome of a given intervention.^{7,9}

In keeping with the gold standard in economic analysis, an incremental cost-effectiveness ratio can be determined based on the ratio of the difference in cost and the difference in outcome of 1 intervention compared with another, aiding in enlightened decisions.⁷ CUA is considered to be most useful in conditions requiring treatment aimed at optimizing quality of life, as would be the case for an invasive ameloblastoma.^{7,9} In view of the current paucity of literature on utility analysis in its surgical treatment and the persistent lack of consensus regarding optimal treatment, this study steered to most accurately obtain such utility values by directly measuring 3 distinct utility scores, thus minimizing the limitations of a single value.

Statistical analysis of the VAS utility measures obtained shows that living with an ameloblastoma during childhood is considered to be less burdensome than what was previously described for unilateral facial paralysis, severe facial disfigurement, binocular blindness, as well as head and neck neoplasms requiring salvage surgery.^{11,12,14} On the other hand, the burden of an ameloblastoma was considered to be greater than that of cleft lip and palate, head and neck neoplasms requiring primary surgery, and of transoral robotic surgery for oropharyngeal cancer.^{13,14,16} Based on these values, one may suggest that resource allocation could be increased for the surgical treatment of pediatric ameloblastomas, considering its greater perceived benefit compared with the 3 aforementioned conditions.

Based on the TTO utility score (TTO = 0.65), the study population would be willing to trade off 28.2 years of life in exchange for a perfect state of health through resection of an ameloblastoma during childhood. Comparing other TTO values reported in the literature, it ranks closer to health than binocular blindness and total laryngectomy with an optimal outcome for laryngeal cancer, but further than that of all other conditions presented in Table 2.¹¹⁻¹⁷ This is striking, as one would be inclined to consider that conditions as serious as severe facial disfigurement requiring facial transplant would yield a lower TTO score than a benign one like ameloblastoma.

A possible explanation for this finding is that unlike the other conditions, the ameloblastoma described in this study involves an affliction during one's youth, which may be considered more burdensome than conditions occurring during adulthood. An alternative explanation is that despite its benignity, an ameloblastoma would inevitably grow slowly, continuously causing more and more morbidity. This is in contrast to both binocular blindness and severe facial disfigurement, which may be considered more serious, but fail to show progression over time. The other explanation may be related to the fact that the scenario presented in this study features an estimated life expectancy of 80 years, compared with the 50 years in the 2 referenced studies. It is possible that one would be willing to trade off more years if expecting a longer lifespan, which is something that could not be controlled for, given the natural history of the condition anticipated in children.

When given the same option to achieve the same outcome as mentioned above, the study population would be willing to risk a hypothetical 35.7% chance of death. This is based upon the ameloblastoma SG utility score (SG = 0.64), which is lower than that of unilateral facial paralysis and severe facial disfigurement, monocular blindness, cleft lip and palate, as well as head and neck cancer surgery, and transoral robotic surgery for oropharyngeal cancer.¹⁶ However, the SG score is greater than that of binocular blindness, locoregional laryngeal, and non-laryngeal head and neck cancers.¹⁷ This is in concordance with the expectation that one would be willing to incur a greater risk of death to treat very debilitating conditions.

Although patients would arguably best understand the implications of the given health state, the decision to recruit participants from the general public is aimed to minimize the inherent conflict of interest. To balance the lack of personal understanding of having an ameloblastoma, participants were provided with ample information about this affliction. The focus on university students, mainly in the medical field, likely contributed to a better comprehension of the health state and of the risks and benefits of the treatment option.⁹

Considering the pediatric focus of this study, one must consider the additional challenges in measuring and applying utility scores among children, developing age-appropriate descriptions, and ethical considerations. It has been demonstrated that 6th grade is the minimum educational level required for the completion of SG and TTO utility surveys.¹⁹ The scenario described featured a 10-year-old child, age at which one would not yet be in 6th grade. Additional are numeracy skills prerequisite to understanding and answering questions as part of utility surveys, as well as the ability to value one's state of health. Instead, this study population was composed of adults asked to imagine themselves as a child in the described health state, known as a proxy, which remains the recommended method of studying child health utility.¹⁹

Limitations of our study include the sample size and the possibility that the study population may not be

representative of society, thereby limiting its applicability for CUA. Although a greater sample size would improve statistical power, this remains the largest study examining utility health measures for the treatment of ameloblastoma. Because we thought that more homogeneous samples would minimize the differences in utility scores, thereby enhancing confidence in results, participants with a medical background were recruited.⁹ Finally, the lack of a post-test survey may also be considered a limitation, as participants' final thoughts with regard to their understanding of the survey or their ease in answering the questions were not elicited.

CONCLUSIONS

The present study shows that a childhood affliction with an ameloblastoma is perceived to be closer to perfect health than that of unilateral facial paralysis, severe facial disfigurement, blindness, and head and neck neoplasms requiring salvage surgery, but farther than cleft lip and palate, head and neck neoplasms requiring primary surgery, and transoral surgery for oropharyngeal cancer. A life expectancy of 28.2 years would be traded off, and a 36% risk of death is deemed acceptable by our study population to undergo surgical treatment for an ameloblastoma during childhood. The objective assessment of the burden of such an affliction by the SG and TTO allows for future use in CUA at a broader population level. Further studies with larger and more diverse samples would add statistical power to utility scores and would be encouraged.

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PATIENT CONSENT

The patient provided written consent for the use of his image.

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