Initial Use of Hierarchically Optimal Classification Tree Analysis In Medical Research

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Initial use of hierarchically optimal classification tree analysis in medicine and allied health disciplines is reviewed.

*Univariate optimal discriminant analysis* (UniODA) is a non-parametric classification methodology for discriminating between two categories of a binary class (“dependent”) variable—such as sex (male versus female), experimental condition (drug versus placebo), or outcome (dead versus alive)—using a single attribute (independent variable). Hierarchically optimal classification tree analysis (CTA) is a non-parametric, non-linear, multiattribute (i.e., appropriate for use with more than one attribute) classification methodology for discriminating a binary class variable, which is accomplished by chaining together successive UniODA models.

CTA and UniODA explicitly maximize model accuracy—operationalized by the effect strength for sensitivity (ESS) index, which is a function of the mean sensitivity achieved by the model across all class categories (the sensitivity of a model for category X is the ability of the model to accurately classify members of category X). For a binary class variable the mean of “sensitivity” and “specificity” (epidemiological terms for model sensitivity for class categories 1 and 0, respectively) is used in computing ESS, which ranges between 0 (the level of accuracy expected by chance) and 100 (errorless classification). By rule-of-thumb, ESS values less than 25 reflect weak effects; values less than 50 indicate moderate effects; and values of 50 or greater reflect strong effects.

CTA was first used in the field of medicine to predict in-hospital mortality attributable to *Pneumocystis carinii* pneumonia, or PCP. Analysis was performed for 1,193 patients discharged alive (N=988) or who died in-hospital (N=205). Manually-derived via UniODA software the CTA model selected as attributes alveolar-arterial oxygen gradient (AaPo₂—difference in partial pressure of oxygen between pulmonary system and blood: higher values indicate more severe pneumonia), body mass index (measure of nutritional status, predictive of poor short- and long-term survival rates), and prior AIDS (binary indicator of whether the current episode of PCP was the first clinical evidence of full-blown AIDS). Illustrated in Figure 1, circles represent model nodes—starting with the root node; Type I error is given beneath each node; arrows indicate decision pathways through the model; values next to arrows indicate UniODA-derived cutpoints; and rectangles represent model endpoints (sample strata), and give the percentage of class 1 observations (people who died) and strata size for the endpoint.
Using the CTA model to classify individual patients is straightforward. For example, imagine a hypothetical 57-year-old patient without prior AIDS had AaPo$_2$=51.1 mm Hg, and body mass index=21.3 kg/m$^2$.

Starting with the root node, since this patient has AaPo$_2$>49.5 mm Hg, the right-hand branch is appropriate. At the next node, since the patient did not have prior AIDS, the left-hand branch is appropriate. Finally, at the next node, because the patient was older than 51.3 Yr, the right-hand branch is appropriate. As seen in Figure 1, 69 patients were classified into the corresponding endpoint presently, and of them one-third—23 patients—died in-hospital.

If the hypothetical patient was younger than 51.3 years then the right-hand branch would have been appropriate, corresponding to an endpoint with 34 patients of whom only three died in-hospital.

Table 1 presents the confusion table summarizing the CTA model overall performance—which is computed by integrating results across all model endpoints. Although the CTA model yielded a relatively weak ESS=21.2, alternative statistical methods used with these data (e.g., logistic regression analysis, regression-based recursive partitioning) achieved ESS values which were less than ten.
Table 1: Confusion Table for Initial CTA Model of PCP Mortality

<table>
<thead>
<tr>
<th>Predicted Mortality Status</th>
<th>Alive</th>
<th>Deceased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual Class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Status</td>
<td>Alive</td>
<td>860</td>
</tr>
<tr>
<td></td>
<td>Deceased</td>
<td>135</td>
</tr>
</tbody>
</table>

Specificity = 87.0%

Sensitivity = 34.1%

Predictive Value

<table>
<thead>
<tr>
<th>Negative</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>= 86.4%</td>
<td>= 35.4%</td>
</tr>
</tbody>
</table>

Staging tables are constructed based upon the findings of a CTA model, as presented for the current example in Table 2. Rows in the staging table are model endpoints reorganized in terms of increasing order of percent of class 1 (dead) membership. Using the staging table to classify individual patients is straightforward. For example, consider the same hypothetical patient discussed earlier, when illustrating how to use the CTA model to classify observations. The staging table is used from left to right. Thus, in the first step of using the staging table, since the patient’s AaPo2>49.5, stages 1, 2 and 6 are inappropriate. In step two, age follows AaPo2 in the staging table and is therefore evaluated next. However, note that for stages 3, 4 and 5—one of which is necessarily appropriate for the hypothetical patient, there are dashes (indicating that one should skip the column) for age. In step three, body mass index is evaluated, but dashes in stages 3-5 indicate this does not apply for the hypothetical patient. In step four Prior AIDS is assessed, and since this patient did not have prior AIDS, stage 5 is inappropriate. Finally, in step five age is re-evaluated, and since the hypothetical patient is older than 51.3 years, stage 4 is appropriate. As seen, of the total of 69 patients classified into stage 4 in the study, \( p_{\text{death}}=0.333 \) (i.e., one-third died in-hospital), and the odds of mortality are 1:2.

Table 2: Staging Table for Initial CTA Model of PCP Mortality

<table>
<thead>
<tr>
<th>Stage</th>
<th>AaPo2</th>
<th>Age</th>
<th>BMI</th>
<th>Prior AIDS</th>
<th>Age</th>
<th>N</th>
<th>( p_{\text{death}} )</th>
<th>Odds_{death}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>\leq 49.5</td>
<td>\leq 49.2</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>602</td>
<td>0.081</td>
<td>1:11</td>
</tr>
<tr>
<td>2</td>
<td>\leq 49.5</td>
<td>&gt; 49.2</td>
<td>&gt; 19.6</td>
<td>-----</td>
<td>-----</td>
<td>34</td>
<td>0.088</td>
<td>1:10</td>
</tr>
<tr>
<td>3</td>
<td>&gt; 49.5</td>
<td>-----</td>
<td>-----</td>
<td>No</td>
<td>\leq 51.3</td>
<td>359</td>
<td>0.231</td>
<td>1:3</td>
</tr>
<tr>
<td>4</td>
<td>&gt; 49.5</td>
<td>-----</td>
<td>-----</td>
<td>No</td>
<td>&gt; 51.3</td>
<td>69</td>
<td>0.333</td>
<td>1:2</td>
</tr>
<tr>
<td>5</td>
<td>&gt; 49.5</td>
<td>-----</td>
<td>-----</td>
<td>Yes</td>
<td>-----</td>
<td>113</td>
<td>0.354</td>
<td>5:9</td>
</tr>
<tr>
<td>6</td>
<td>\leq 49.5</td>
<td>\leq 49.5</td>
<td>\leq 19.6</td>
<td>-----</td>
<td>-----</td>
<td>16</td>
<td>0.438</td>
<td>3:4</td>
</tr>
</tbody>
</table>
Stage is an ordinal index of severity of illness, and \( p_{\text{death}} \) is a continuous index: increasing values on either of these indices indicate worsening disease. Compared to the first and second stages, the third stage reflects a 2.7-fold difference in the likelihood of dying in-hospital; stages four and five reflect a 4-fold difference; and stage six reflects a 5.2-fold difference in the likelihood of dying in-hospital.

Subsequent research using the ordinal severity staging algorithm to create a prognostic index has confirmed stage as a powerful ordinal risk factor for in-hospital mortality from PCP.\(^4,5\)

Recently, with increasing use of PCP prophylaxis and multidrug antiretroviral therapy, the clinical manifestations of HIV infection have changed dramatically. Because predictors of inpatient mortality for PCP may have also changed, CTA was used to develop a new staging system for predicting inpatient mortality for patients with HIV-associated PCP admitted between 1995 and 1997.\(^6\) Chart reviews were performed for 1,660 patients hospitalized with HIV-associated PCP at 78 hospitals in seven metropolitan areas in the USA. CTA identified a five-category staging system (ESS=33.1) using three predictors: wasting, alveolar-arterial oxygen gradient (AaPO\(_2\)), and serum albumin level. Mortality rate increased with stage: 3.7% for Stage 1; 8.5% for Stage 2; 16.1% for Stage 3; 23.3% for Stage 4; and 49.1% for Stage 5.

During the mid-1990s, community-acquired pneumonia (CAP) began to account for an increasing proportion of the pulmonary infections in people with HIV infection: hospital mortality rates for HIV-associated CAP ranged to 28%. A staging system was thus developed for categorizing mortality risk of patients with HIV-associated CAP using information available prior to hospital admission.\(^7\) The data were based on a retrospective medical records review of 1,415 patients hospitalized with HIV-associated CAP from 1995 to 1997 at 86 hospitals in seven metropolitan areas. The overall inpatient mortality rate was 9.1%. Predictors of mortality in the CTA model included presence of neurologic symptoms, respiratory rate of 25 breaths/minute or greater, and creatinine>1.2 mg/dL. A five-category staging system was identified, yielding a mortality rate of 2.3% for stage 1, 5.8% for stage 2, 12.9% for stage 3, 22.0% for stage 4, and 40.5% for stage 5: ESS=45.5. It was concluded that the staging system is useful for guiding clinical decisions about the intensity of patient care, and for case-mix adjustment in research addressing variation in hospital mortality rates.

CTA was also used to discriminate CAP versus inhalational anthrax cases.\(^8\) Limiting the effects of a bioterrorist anthrax attack necessitates rapid detection of the earliest victims, so a study was conducted to improve physicians’ ability to rapidly detect inhalational anthrax victims. A case-control study compared chest radiograph findings from 47 patients from historical inhalational anthrax cases and 188 community-acquired pneumonia control subjects. CTA was used to derive an algorithm of chest radiograph findings and clinical characteristics that accurately discriminated between inhalational anthrax and community-acquired pneumonia. A nearly perfect CTA model (ESS=98.3) involving three attributes (chest radiograph finding of mediastinal widening, altered mental status, and elevated hematocrit) was 100% sensitive (95% confidence interval [CI], 73.5% to 100%) and 98.3% specific (95% CI, 95.1% to 99.6%).

The most recent investigation in this line of research used CTA to derive an algorithm for emergency department (ED) triage for rapid ordering of chest radiography for CAP, which accounts for 1.5 million annual ED patient visits in the US.\(^9\) An ED-based retrospective matched case-control study was conducted with 100 radiographic confirmed CAP cases and 100 radiographic confirmed influenza-like-illness controls. A CTA model was obtained that used three attributes (temperature, tachycardia, and hypoxemia on room air pulse oximetry), which
was 70.8% sensitive (95% CI=60.7% to 79.7%) and 79.1% specific (95% CI=69.3% to 86.9%): ESS=49.9.

Encouraged by the initial and continuing success of CTA in modeling heretofore poorly-understood outcomes, the use of CTA began to proliferate across a variety of substantive areas within medicine. Areas of representation may be broadly categorized as representing clinical medicine, psychosocial aspects of medicine, and allied health disciplines. Research using CTA in these areas is reviewed below.

**Clinical Medicine**

CTA has been used in clinical medicine applications such as predicting adverse drug events (ADEs) using hospital administrative data in exploratory data-mining research, and pharmacoalgorithmics in confirmatory theory-building research; self-selection for interventional management on the basis of clinical and psychosocial factors; gestational age at delivery after placement of an emergent cerclage; and mortality from thienopyridine-associated thrombotic thrombocytopenic purpura, as well as from complications of HIV on the basis of nutritional information for a large observational database.

Hospital administrative data are appealing for surveillance of ADEs because of their uniform availability, but expert-generated surveillance rules have limited accuracy. To assess whether rules based on nonlinear associations among available administrative data are more accurate, CTA was applied to administrative data, and used to derive and validate surveillance rules for predicting bleeding/anticoagulation and delirium/psychosis ADEs. Using a retrospective cohort design, a random sample of 3,987 patient admission records were drawn from all 41 Utah acute-care hospitals: reviewers identified ADEs using implicit chart review; pharmacists assigned Medical Dictionary for Regulatory Activities codes to ADE descriptions for identification of clinical groups of events; and hospitals provided patient demo-

graphic, admission, and ICD-9-CM data. Incidence proportions were 0.8% for drug-induced bleeding/anticoagulation problems and 1.0% for drug-induced delirium/psychosis. The CTA model for bleeding had very good PAC (87%) and sensitivity (86%), and fair positive predictive value (12%). The CTA model for delirium had excellent sensitivity (94%) and PAC (83%), but low positive predictive value (3%). Poisoning and ADE codes designed for targeted ADEs had low sensitivities, and degraded model accuracy when forced in. These findings indicate that CTA is a promising method for rapidly developing clinically meaningful surveillance rules for administrative data. The resultant model for drug-induced bleeding and anticoagulation problems may be useful for retrospective ADE screening and rate estimation.

In contrast to the preceding classical exploratory data-mining application of CTA to study ADEs, Belknap began with the axiom that a prescription may be conceptualized as a health-care program implemented by a physician in the form of instructions that govern the plan of care for an individual patient. Using software design principles and debugging methods were used to create a “Patient-oriented Prescription for Analgesia” (POPA), the rate and extent of adoption of POPA by physicians was assessed, and CTA was conducted to evaluate whether POPA would reduce the rate of severe and fatal opioid-associated ADEs. The study involved a population of 153,260 hospitalized adults, 50,576 (33%) of whom received parenteral opioids. Hospitalwide, the use of POPA increased to 62% of opioid prescriptions, and opioid-associated severe/fatal ADEs fell from an initial peak of seven/month to zero/month during the final six months of the study.

In a study of treatment bias in observational outcomes research, CTA was used to assess the role of clinical and psychosocial factors in predicting self-selection for interventional management (lower extremity bypass surgery or angioplasty) for patients with intermittent clau-
A total of 532 patients with mild to moderate lower extremity vascular disease, without prior peripheral revascularization procedures or symptoms of disease progression, were enrolled in a prospective outcomes study at the time of an initial referral visit for claudication to one of 16 Chicago-area vascular surgery offices or clinics. Study variables were derived from lower extremity blood flow records and patient questionnaires, and follow-up home health visits were used to ascertain the frequency of lower extremity revascularization procedures within six months (13.3%). Ten patient attributes were used in the CTA model: sensitivity=67.6%; specificity=92.9%; relatively strong ESS=57.7%. Initial ankle-brachial index (used to classify 100% of sample), leg symptom status over the previous six months (used to classify 89% of sample), self-reported community walking distance (used to classify 74% of sample) and prior willingness to undergo a lower extremity hospital procedure (used to classify 39% of sample) were the most influential attributes in the model, and are critical control variables for a valid observational study of treatment effectiveness.

CTA was also used to develop a predictive model for predicting gestational age at delivery, after placement of an emergent cerclage in the second trimester, for 116 women with documented cervical change on physical examination. CTA was used to predict delivery prior to 24 weeks, between 24 and 27 6/7 weeks, or 28 weeks or later. Delivery prior to 24 weeks was best predicted by presence of prolapsed membranes and gestational age at cerclage placement; delivery between 24 and 27 6/7 weeks was best predicted by parity alone; delivery of at least 28 weeks was best predicted by cervical dilation and length, presence of prolapsed membranes, and parity. When choosing a single model to predict delivery at the three different gestational age periods, the model predicting delivery at 28 weeks yielded the most accurate results. These findings indicated that CTA-based predictive models for outcome after emergent cerclage are informative for both patients and physicians.

CTA was also used in recent research describing clinical and laboratory findings for a sample of 128 patients with thienopyridine-associated thrombotic thrombocytopenic purpura (TTP). Duration of thienopyridine exposure, clinical and laboratory findings, and survival were recorded for all subjects, and ADAMTS13 activity (39 patients) and inhibitor (30 patients) were measured for a subset of individuals. Among patients who developed TTP more than two weeks after thienopyridine exposure, therapeutic plasma exchange (TPE) increased likelihood of survival (84% versus 38%, p<0.05). In contrast, among patients who developed TTP within two weeks of starting thienopyridines, survival was 77% with TPE and 78% without. Findings suggested that TTP drug toxicity occurs by two different mechanistic pathways, characterized primarily by time of onset before versus after two weeks of thienopyridine administration.

A large, retrospective, observational database containing detailed medical records on 2,179 HIV-positive patients who attended the Johannesburg General Hospital HIV clinic was mined to assess the effect of nutrition on health in this population. Times to progression or death were calculated from the patient's first clinic visit. CTA showed that by using race alone, one can predict progression to AIDS in ≤1 year for 79.3% of nonwhite patients, and predict no progression for 59.4% of white patients. For nonwhite patients, the next most useful predictor of progression was the use of multivitamins: multivitamin tablets (MVI), vitamin B complex tablets (VBC), or pyridoxine used in the clinic. The median progression time to AIDS was 32.0 weeks for patients without vitamins and 72.7 weeks for patients who took vitamin B, and the median survival was 144.8 weeks for patients without vitamins and 264.6 weeks for patients who took vitamin B. These findings
demonstrate that CTA can elucidate clinically-relevant relationships within large patient populations, such as observational databases.

Finally, CTA was used to identify risk factors for venous thromboembolism (VTE) during the rehabilitation phase of spinal cord injury for a sample of 243 patients with acute spinal cord injury, 51 of whom had VTE, and 8 of whom died.\(^\text{17}\) Attributes included type and location of spinal cord injury, American Spinal Injury Association classification, concomitant injuries, surgical procedures, complications, preexisting illnesses, and use of antithrombotic prophylaxis. A three-attribute CTA model identified patient groups differing in likelihood of experiencing deep vein thrombosis (DVT). The group having the highest likelihood of DVT was patients with cancer over the age of 35 years, though women without cancer between the ages of 36 and 58 years, as well as cancer-free men with flaccid paralysis, were also at increased risk.

**Psychosocial Aspects of Medicine**

CTA has been used in the study of psychosocial aspects of medicine, such as quality-of-care and patient satisfaction in the emergency department; severity-of-illness and quality-of-life among asthma patients; age and functional status of ambulatory internal medicine patients; and literacy and hospitalization rates of general medicine outpatients.

For example, CTA was used to identify perceptions that predict patient (dis)satisfaction with Emergency Department (ED) care.\(^\text{18}\) Data were responses: (a) to a survey mailed to all discharged patients over a 6-month period (Academic Hospital); or (b) to a telephone-based interview of a random sample of discharged patients over a 1-year period (Community Hospital). The survey and interview both assessed overall satisfaction, and satisfaction with perceived waiting times, information delivery, and expressive quality of physicians, nurses, and staff. Data for 1,176 patients (training sample) and 1,101 patients (holdout sample) who rated overall satisfaction as either “very good” or “very poor” (Academic Hospital), and for 856 patients (training sample) and 431 patients (holdout sample) who rated overall satisfaction as either “excellent” or “poor” (Community Hospital), were retained for analysis. For both hospitals, CTA models efficiently achieved ESS values \(\geq 90\) (all \(p<0.0001\)). The findings reveal that overall (dis)satisfaction with care received in the ED is nearly perfectly predictable on the basis of patient-rated expressive qualities of ED staff, and suggest that interventions designed to reinforce positive expressive provider behaviors may reduce the number of dissatisfied patients by half.

CTA was also used to associate severity-of-illness (assessed using the Asthma Severity Index, or ASI) with quality-of-life (QOL) in a prospective study of clinical and psychological correlates of adverse asthma outcomes.\(^\text{19}\) Data, collected at study intake and then every three months thereafter for a year from 13 adults with asthma, included a QOL scale, an ASI survey, spirometry, and history and physical exam. A perfect CTA model was identified which included a query about bodily pain in the last four weeks, and a self-assessment of general health.

Research reporting the first CTA ever published discriminated 65 geriatric (\(\geq 65\) years of age) and 85 non-geriatric ambulatory medical patients using five functional status subscales, and five single-item measures hypothesized to be relevant to functional status (assessing physical limitations, social support, and satisfaction with health).\(^\text{20}\) Results revealed four strata (“patient clusters”): relatively active nongeriatric adults; relatively inactive geriatric adults; inactive, depressed, socially isolated young women; and active, happy, socially connected geriatric adults.

Higher hospitalization rates have been reported among patients with low literacy, but prior research neither determined the preventability of these admissions, nor considered other
determinants of hospitalization, such as social support. CTA was used to evaluate whether low literacy is a predictor for preventability of hospitalization when considered in the context of social support, sociodemographics, health status, and risk behaviors, for a sample of 400 patients admitted to general medicine wards in a university-affiliated Veterans Affairs hospital. Two board-certified internists independently assessed preventability of hospitalization and determined the primary preventable cause through blinded medical chart reviews. Significant predictors of having a preventable cause of hospitalization included binge alcohol drinking, lower social support for medical care, three or fewer annual clinic visits, and 12 or more people talked to weekly.

Allied Health Disciplines

CTA has been used in research in allied health disciplines, including studies designed to enhance psychological diagnostic accuracy, model psychosocial adaptation, improve long-term functional status, and predict adolescent psychiatric inpatient hospitalization.

The utility of the Behavioral Assessment System for Children (BASC) and Child Behavior Checklist (CBCL) Parent scales was assessed in terms of discriminating between: (a) students with attention deficit-hyperactivity disorder (ADHD) versus non-ADHD students, and (b) inattentive-type versus combined-type ADHD-afflicted students. For both the BASC and the CBCL, a different CTA model was developed for each of the two diagnostic predictions. For distinguishing ADHD versus non-ADHD students the BASC model was more parsimonious and accurate than the CBCL model, whereas for differentiating between inattentive versus combined types the CBCL model was superior. The results demonstrate the diagnostic utility of the BASC and CBCL, and describe salient behavioral dimensions associated with subtypes of ADHD. A Bayesian methodology for estimating the efficiency of a CTA model versus chance, for any given base-rate of class 1 (and also of class 0) membership, is presented.

In a conceptually similar study, demographic and clinical correlates of lifetime substance use disorders were studied in a cohort of 325 recently hospitalized psychiatric patients. Gender (male), age (younger), education (less), time in jail, conduct disorder symptoms, and antisocial personality disorder symptoms were predictive of substance use disorders. CTA was successful in predicting 74% to 86% of the alcohol, cannabis, and cocaine use disorders.

CTA was used to examine how individual- and family-level predictors in late childhood and preadolescence relate to psychosocial adaptation (i.e., scholastic success, social acceptance, and positive self-worth) in early adolescence. A prospective study included 68 families of children with spina bifida, and 68 comparison families of healthy children. Multi-method, multi-informant data were evaluated via CTA. Factors best predicting psychosocial adaptation in early adolescence included intrinsic motivation, estimated verbal IQ, behavioral conduct, coping style, and physical appearance: ESS=56.2. There were no significant group (spina bifida versus able-bodied) effects. These results suggest that processes leading to psychosocial adaptation may be similar for youth with and without chronic illness.

Seventy patients with chronic fatigue syndrome were randomly assigned to the control (N = 33) or experimental (N = 37) group. All patients continued usual medical care, but experimental subjects underwent a 9-week-long, 2-hours-per-week training in mindfulness meditation and medical qigong practices. CTA was used to model change in SF36 12-month Health Transition score: patients were categorized as “improvers” versus “non-improvers”. The model achieved very strong ESS = 80.5, based on SF36 Role Functioning Physical score and frequency of mind/body self-healing practice. Another conceptually related study suggests that
ipsative transformations of functional status measures may be the preferred pre-processing strategy for designs involving the use of longitudinal data.26

Finally, CTA was used to explore predictors of inpatient hospital admission decisions for a sample of 13,245 children in foster care over a four-year period.27 As hypothesized, clinical variables including suicidality, psychoticism and dangerousness predicted psychiatric admissions; however, family problems, and the location of hospital screening, impacted decision making in a subsample of cases. The CTA model developed in Year 1 reliably and consistently predicted admission decisions across the next three years.

Conclusion

CTA has produced the most powerful models yet published in the applications in which it has been employed in the field of medicine. Research ongoing over the span of a decade also showed that CTA models replicated across time better than had any prior models of the pulmonary phenomena under study. This result is encouraging, particularly since most published research using CTA reported models derived manually using UniODA software, with model growth controlled using a sequentially-rejective Bonferroni-type procedure to guard against alpha inflation and model overfitting.20

Recently, however, an optimal pruning methodology has been developed which examines all possible subtrees of the final CTA model, and explicitly identifies the model which maximizes ESS while maintaining control of the experimentwise Type I error rate.21,2 The use of pruning to maximize ESS was illustrated for the example presented earlier, involving predicting in-hospital mortality of AIDS patients with PCP.28 Compared to the non-pruned model (see Figure 1), in the pruned (maximum ESS) CTA model no attributes emanated from the right-hand-side of the tree: Prior AIDS and Age were dropped. The pruned CTA model achieved ESS of 33.7, representing a moderate effect (versus the relatively weak effect yielded by the non-pruned model), and reflecting a 59% increase in ESS. Compared to the non-pruned model (see Table 1), the optimized model had 32.1% lower specificity, but 118.8% greater sensitivity; and 6.2% greater negative predictive value, but 28.7% lower positive predictive value. In addition, the optimized model used one fewer node than the non-pruned model, rendering it 98.7% more efficient than the non-pruned model—averaging 8.4 versus 4.24 ESS-units-per-attribute, respectively.1

Software capable of conducting automated CTA became commercially available in fall, 2010 (www.OptimalDataAnalysis.com).29 Beyond obvious savings in time and labor, two primary advantages of automated CTA both involve pruning. First, when the CTA model is derived manually the Bonferroni procedure is conducted as the model is grown. After model growth is completed, attributes in close proximity to the root variable, having \( p \approx 0.05 \), may be forced out of the model as an increasing number of attributes load on lower branches, disrupting the model and the modeling process. When conducting automated analysis the associated recursive trimming and re-development process is user-transparent: the computer simply executes the algorithm. Second, automated software always conducts pruning to explicitly maximize model accuracy, a task which becomes difficult to accomplish manually for complex models.2

A powerful feature of the automated CTA software is an enumeration command, which specifies that all combinations of attributes in the top three nodes will evaluated. For example, an enumerated CTA analysis was conducted using the same attributes and data which were available for prior logistic regression, recursive partitioning analyses, and manually-derived CTA, in the PCP mortality example.28 Using two attributes—total lymphocyte count as the root (with three emanating branches) and
AaPo2 (used on two branches)—the enumerated CTA model achieved 69.5% sensitivity, 70.1% specificity, moderate ESS=39.7 (17.8% greater than for the pruned manually-derived CTA model), and good efficiency=13.2 ESS units-per-attribute (17.9% greater than for the pruned manually-derived optimized manual model).

Several additional features of the automated CTA platform29 set the stage for an interesting “second round” of application of CTA in medicine and allied health disciplines. For example, a forcenode command forces CTA to insert the attribute var at node node in the solution tree—useful for confirmatory modeling. Also, a minimum denominator command allows specification of minimum endpoint sample size (useful to ensure statistical power); a minimum sample size command forces the solution to classify some specified minimum sample size (useful in data sets involving many missing values); and a maximum depth command limits the depth that the CTA model may achieve (useful for identifying efficient models). Time will tell if enhanced precision and flexibility will yield even more powerful models than have been reported in the first “manual” round of application of CTA in the field of medicine.

References


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**Author Notes**

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