Screening for prostate cancer: A decision analysis

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Overall objective: To determine optimal screening policies for prostate cancer at the levels of populations, sub-groups, and individuals.

Population analysis

Base-line questions:

* What would be the effect on the population if all men were screened *annually* by the PSA+ as opposed to conventional digital rectal examination?

* How would these results be affected by (a) differential rates of compliance with the two types of tests, and (b) if the PSA+ could be made more effective?

Timing and types of tests:

* What would be the effects on the population if testing was not conducted annually, but according to some other schedule -- varying frequency and frequency according to age?

* What would be the effects of varying frequency, frequency by age, and types of tests?

* How do screening policies interact with different treatment policies?

Economic analysis:

* How are the above strategies affected by the costs of testing? Which provide the greatest benefits relative to costs?

Sub-group analysis

* What are the implications of the above questions for sub-groups broken down by, say, age? For example, should testing policy be different for men in their 50's, 60's and 70's?

Individual analysis

* Recommendations for individuals suffering from other conditions.

Research strategy

1. Develop and test model on 1987 data.

2. Use model to predict effects in terms of estimated future populations.

3. Extensive use of sensitivity analysis for both testing and predicting.

Underlying model

1. Markov process assumed to model progression of disease.

2. Decision tree used to model implications of different testing and treatment strategies.

3. Accounting process to keep track of year-by-year effects on population.

Markov model

Six pathological states are assumed:

1. No cancer
2. Cancer A
3. Cancer B
4. Cancer C
5. Cancer D
6. Dead

Disease must progress sequentially through each of the stages.

Every 6 months, there is a chance that a person will move from one stage to the next. Thus, it is possible that someone with No cancer could reach stage D in 2 years. On average, however, it is likely to take much longer.

All but one of the transition probabilities (i.e., chances of moving between stages) are assumed constant and thus independent of age. The exception is from No cancer to Cancer A which is assumed to increase with age.

Decision tree

No matter what tests are used, tree has identical structural assumptions:

1. Symptomatic or asymptomatic.

2. Go for an exam or don't go for an exam.

3. If don't go for an exam, could subsequently be examined during a routine check-up.

4. Men can refuse to undergo biopsy after positive test results.

5. If exam results are negative, men can undergo TURP which can lead to the diagnosis of cancer.

6. Following diagnosis, patients are staged and assigned a clinical state A, B, C, or D which may or may nor correspond to their true state. There are several treatment options that vary by stage of the disease as staged and by age.

7. Different complications are considered following treatment. These include death from treatment itself. Probabilities of death by treatment depend on type of treatment.

8. Some probabilities are assumed to be age-dependent, e.g., concerning whether men are symptomatic and type of treatment.

9. Treatment is either effective or ineffective. If treatment is effective, men are assumed to be in the No cancer group until they die from other causes. Probabilities of effective treatment vary by stage of the disease.

Parametric assumptions - - estimated from medical literature or expert opinion

1. Symptoms

   a. Probabilities of symptoms/no symptoms given different diseases states (i.e., No cancer, A, B, C, D).

   b. Probabilities of having a TURP given presence/absence of symptoms and different disease states.

2. Behavioral

a. Probabilities of undergoing a test given presence/absence of symptoms and different disease states.

b. Probabilities of undergoing a test during a routine medical given presence/absence of symptoms and different disease states.

c. Probability of accepting biopsy after positive test results.

3. Test specificity/sensitivity

a. PSA+

b. Digital rectal examination

c. Biopsy

d. TURP

e. Staging: relation between true and clinical states

4. Treatment

a. Probabilities of types of treatment by states of disease and age.

b. Probabilities of different types of complications.

c. Probabilities of effectiveness of treatments by states.

Developing and testing model

1. Initial model is run by "following" a cohort of 50-year old men over a 44-year period.

2. As specified above, assumptions are made concerning several structural parameters, e.g., probabilities of going for an exam, test specificities and sensitivities, etc. Data are then used to estimate key parameters, namely:

* The distribution of underlying stages of the disease at early ages.

* The transition probabilities of the underlying Markov process, i.e.,
  NC to A
  A to B
  B to C
  C to D
  D to Death

and the NC to A increase with age coefficient.

The data used to fit the model are:

1987 age-specific cancer death rates (year-by-year)

Data on stage-specific cancer incidence rates (5-year intervals)

Data on autopsy-based prevalence (10-year intervals -- poor)

Swedish longitudinal data

Data on TURPs

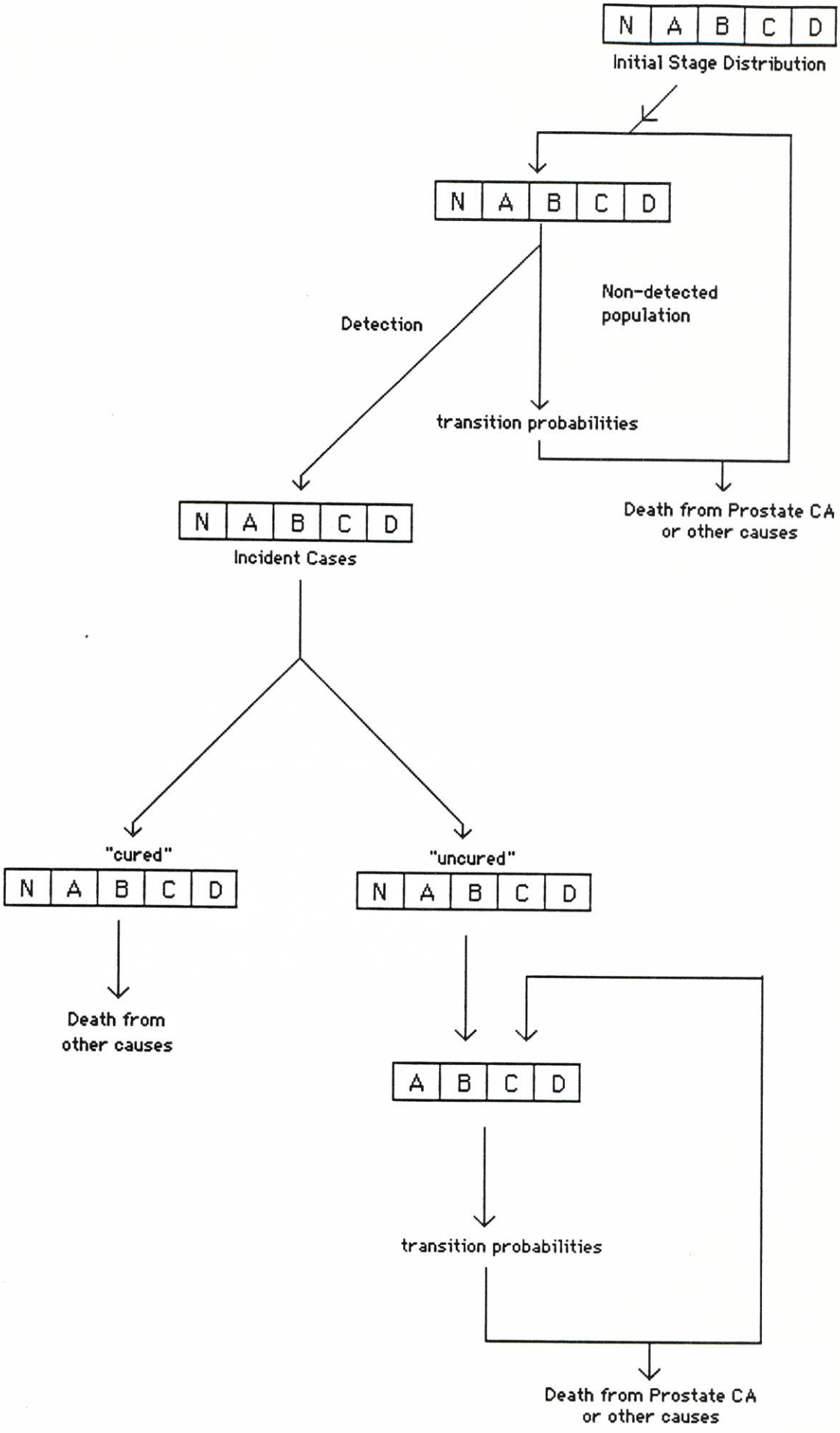
Preliminary results

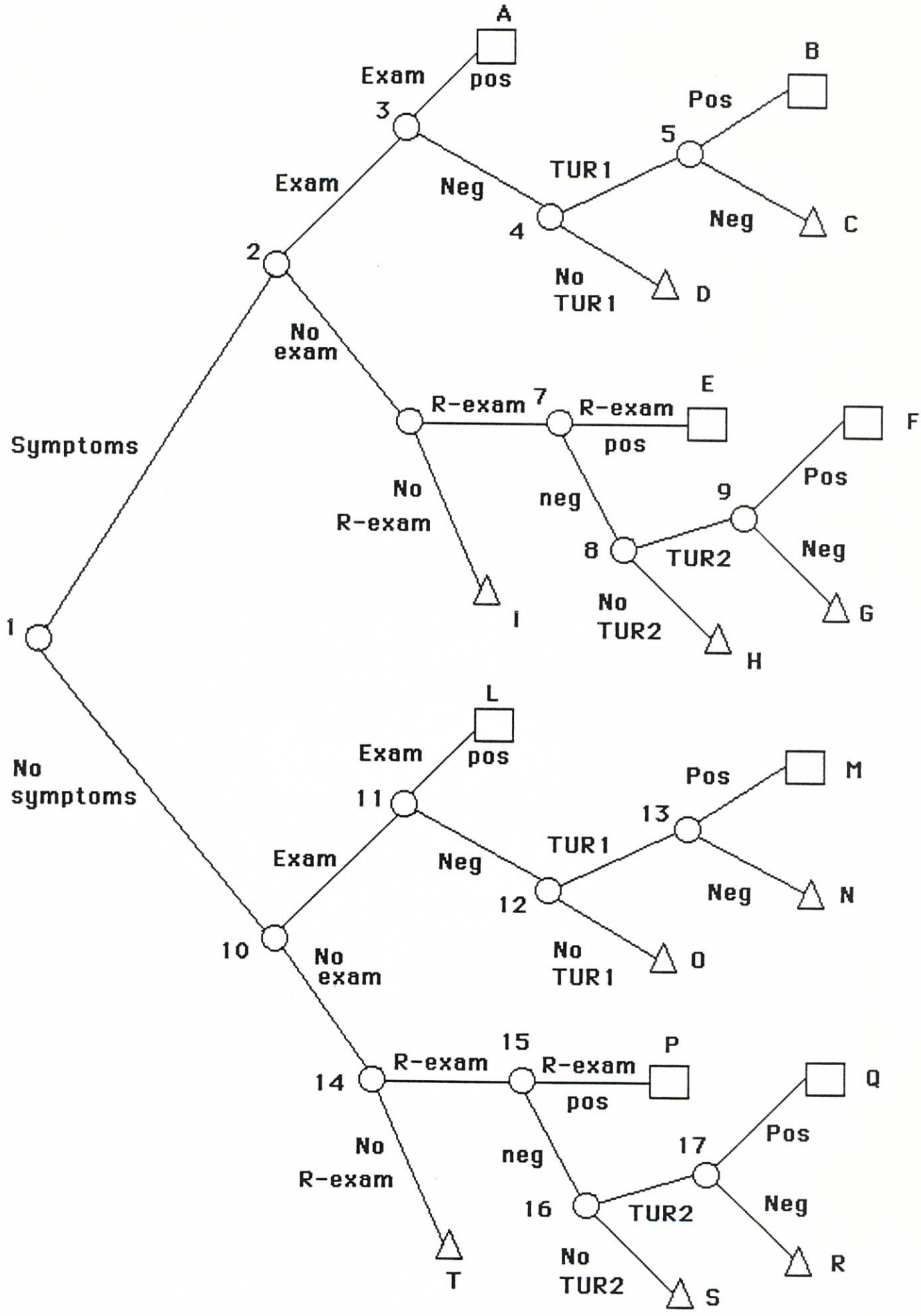
* Fitting death rates per year on 1987 data (shows need for more data!)

* Illustrations:

  Effects of varying different parameters

  Effects of different tests (what would have been)


N A B C D
Initial Stage Distribution
N A B C D
Non-detected
population
Detection
transition probabilities
Death from Prostate CA
or other causes
N A B C D
Incident Cases
"cured"
N A B C D
"uncured"
N A B C D
Death from
other causes
A B C D
transition probabilities
Death from Prostate CA
or other causes


A
Exam
pos
3
B
Pos
5
Exam
TUR1
Neg
Neg
C
4
2
No
TUR1
D
No
exam
R-exam
7
R-exam
E
pos
F
Symptoms
No
R-exam
neg
9
Pos
8
TUR2
Neg
No
TUR2
G
1
I
H
L
Exam
pos
No
symptoms
11
Pos
M
13
TUR1
Exam
Neg
Neg
N
12
10
No
exam
No
TUR1
O
15
R-exam
P
R-exam
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pos
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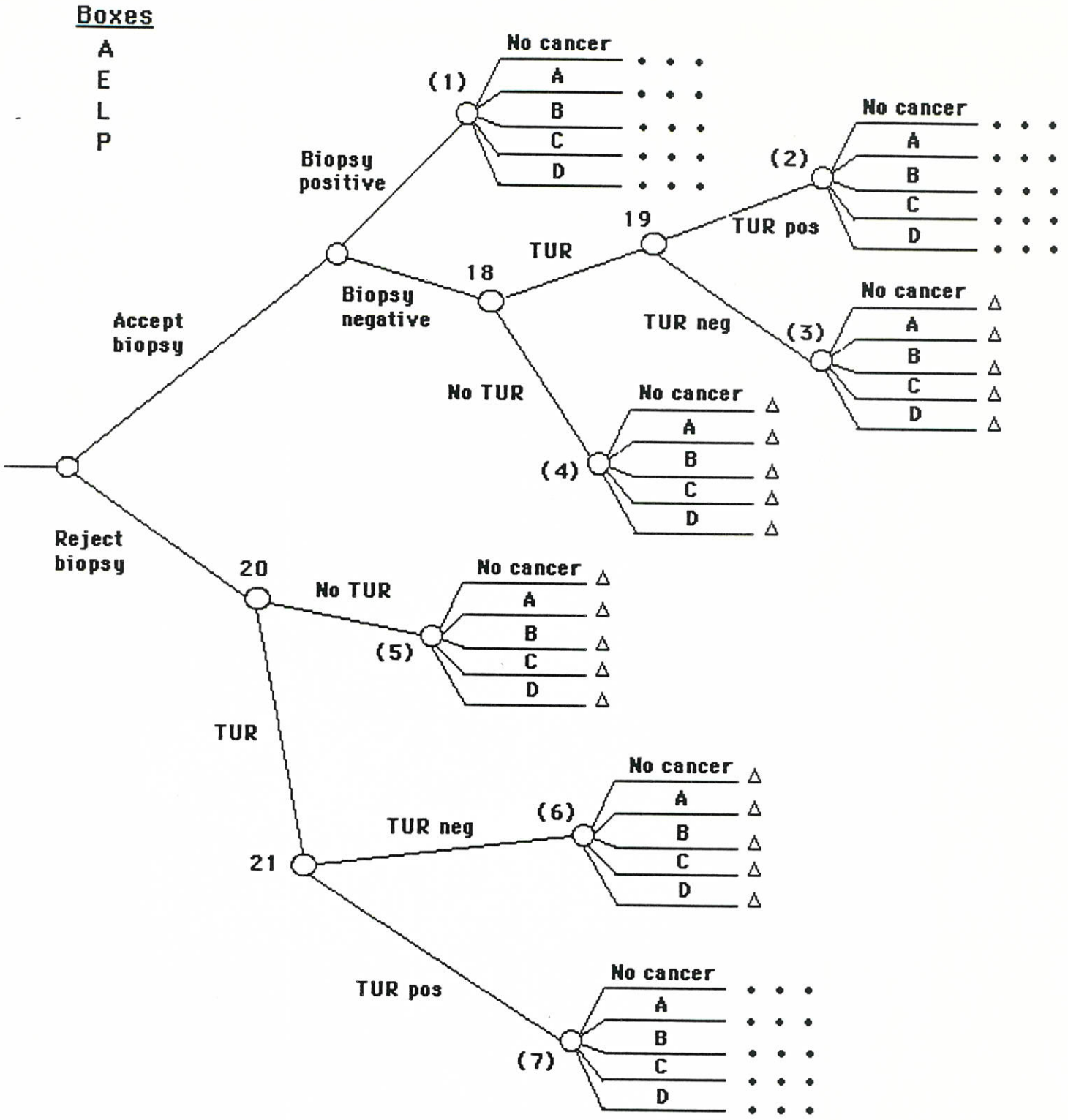
17
Pos
16
TUR2
Neg
No
TUR2
R
T
S



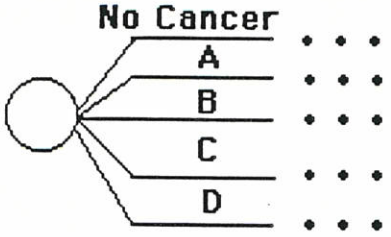
Staging, treatment, complications, cures.

End states

Numbers, both with and without parentheses, correspond to points of the computer program.

Boxes

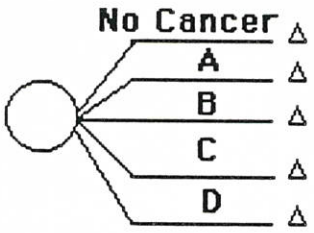
B
F
M
Q



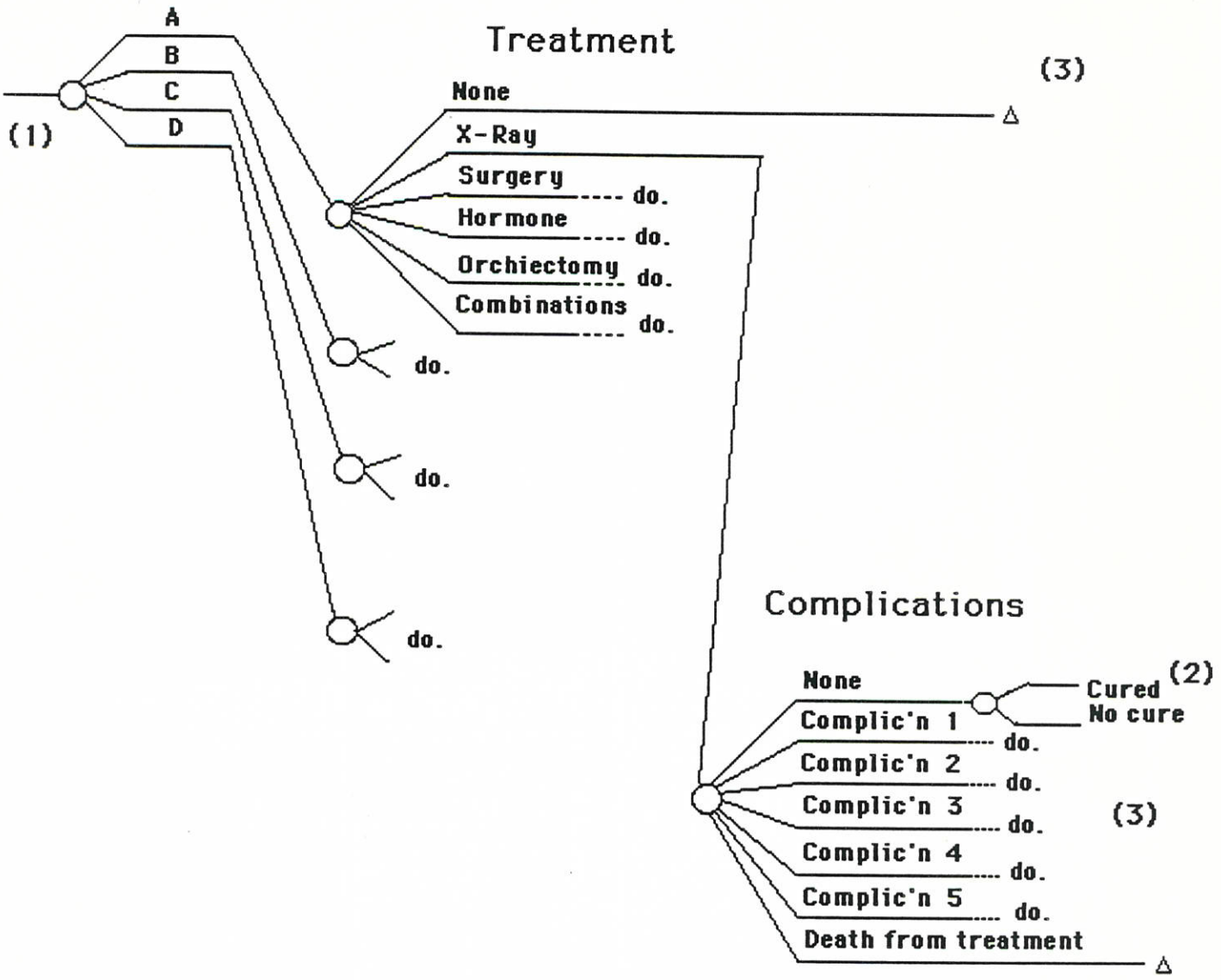
Staging, treatment, complications, cures.

Triangles

C N
D O
G R
H S
I T



Staging by clinical states



Notes: (1) Pattern repeats for NC, A, B, C, and D.
(2) Probability of cure depends on effectiveness of cure and true state
(3) At end of tree, clinical states are transformed back to true states.