Empirical Treatment of Chronic Cough
A Cost-Effectiveness Analysis

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Abstract

Chronic cough of unknown etiology is often difficult to diagnose, thus, there exists controversy regarding the management of such patients. Although the ACCP (American College of Chest Physicians) statement in 1998 recommended that treatment should follow testing, recent evidence suggests that empirical treatment of GERD is more cost-effective than testing followed by treatment, in both chronic cough and non-cardiac chest pain. In this paper, we evaluated the cost-effectiveness in managing patients with chronic unexplained cough by building a decision model, and compared the cost-effectiveness of six most common management strategies. The outcome of our analysis demonstrates that empirical treatment is the cheapest option, while testing followed by treatment is the most expensive option with the shortest time course.

1 Introduction

Cough is one of the most common clinical problems that may be caused by a large number of diseases. It can be defined as acute or chronic based upon the cough duration - the duration for acute cough is three weeks or less, and the duration for chronic cough is three weeks or more.

After initial investigations which eliminate obvious causes of chronic cough such as chronic bronchitis, pulmonary tuberculosis, lung cancer, and treatment with angiotensin converting enzyme (ACE) inhibitor drugs, we are left with a group of patients who are non-smokers, not taking ACE inhibitor, and having normal chest roentgenogram. These patients who are suffering from chronic unexplained cough are mostly caused by post-nasal drip syndrome (PNDS), asthma, and/or gastroesophageal reflux disease (GERD). As in accordance with some published studies such as [1] found PNDS in 41% of the cases; asthma, 24%; and GERD, 21%.

Amongst the various plausible management strategies for patients with chronic unexplained cough, the ACCP (American College of Chest Physicians) proposed testing followed by treatment. However, recent studies [2] [3] suggested that empirical treatment of GERD is more cost-effective than testing followed by treatment in both chronic cough and non-cardiac chest pain. Nevertheless, the cost-effectiveness of an overall empirical treatment strategy for chronic cough has not been studied previously.

Decision analysis is a structured approach to making important decisions. It has developed from a mathematical theory to a discipline that is widely used in many industries and professions, such as engineering, medicine and government agencies. In this paper, we used decision analysis concepts and tools to build a decision model and evaluate the cost-effectiveness of a variety of management strategies which include combined testing, combined treatment, sequential treatment, sequential testing, and different combinations of testing and treatment. All models were constructed and analyzed using DATA 3.5 [4] software.

2 The Model

In building our decision model, influence diagram [5] and decision tree were used to structure the elements of the decision situation into a logical framework. So that we could obtain a complete model of the decision problem with clear demonstration of the relevant objectives, decisions to make, uncertainties, and consequences. Figure 1 shows the influence diagram of the model. The decision node *Strategy*, consists of an enumerated list of alternatives that can be used by clinicians to manage patients with chronic unexplained cough. The chance nodes contain a list of possible outcomes to each uncertainty, and each of the deterministic nodes holds a state constant or variable. The value node stores the utility or payoff to each outcome.

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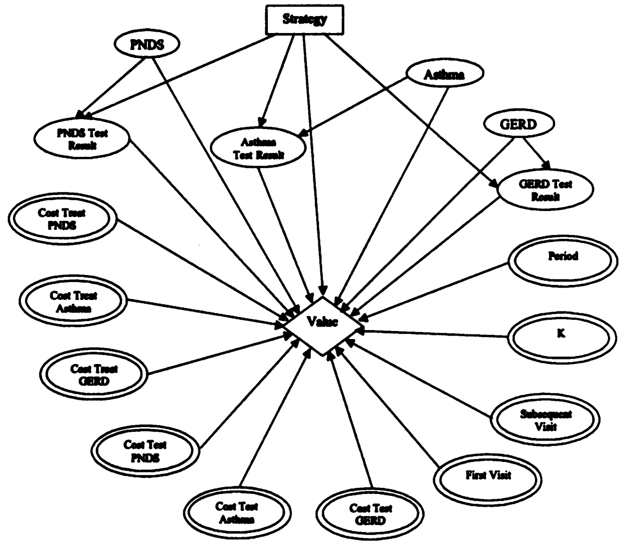


Figure 1: Influence Diagram

Decision Strategies In spite of the existence of myriad strategies for the management of patients with chronic cough of unknown etiology, not every strategy will arouse equal interest of the clinicians. Six alternative management approaches were arrived at by consensus among several clinicians who regularly manage patients with this problem. Among the strategies selected are, 1)Test All Then Treat, which was suggested by ACCP, 2)Treat All, which was found to be efficient in some studies for GERD [2] [3], 3)Treat PNDS Test Asthma Treat GERD, which was claimed to be efficient by [6], 4)Treat Sequentially Starting With PNDS, 5)Test Then Treat Sequentially, and 6)Treat PNDS Test Asthma And GERD Together.

State Constants, Variables, and Assumptions The assumed prevalence and test performance for each condition/disease in the model was representative of reports in the literature and experience in the local population. Sensitivity analysis was later performed on these variables to assess the impact on the decision model as the values of these variables change. The values of the state constants and variables can be found in Figure 2. Several assumptions were also made when building the decision model.

1. The occurrences of the three diseases are independent.
2. The maximum treatment period for each strategy is 12 weeks.
3. The entire duration from getting a test and obtaining the test outcome is one week, based on the current practice in this country.
4. It takes at most two weeks to see the effect of a treatment drug on a patient.
5. The treatment drugs are 100% effective. This parameter is not a critical factor in this case study.

3 Calculation of Expected Cost

The expected cost or Total Cost of each strategy is the sum of Direct Cost and Indirect Cost. The Direct Cost is the costs of consultation, treating and testing of PNDS, Asthma and GERD. The Indirect Cost is the costs that are borne by the patients in the form of opportunity cost of inconvenience caused by coughing. Indirect Cost may be incurred by the use of wrong treatment strategy or inefficient treatment strategy thereby prolonging the duration of cough.

The Indirect Cost is an increasing function. We approximate it with a simple function, $U(x) = K \times x^a$, where the parameter $a > 0$ indicates the degree of averseness of a patient towards prolonged cough, $K > 0$ is the cost of coughing for the first week, and x is the duration of cough in terms of weeks. When $a > 1$, the patient is averse to cough and exhibits increasing marginal cost with cough duration and this is represented by a convex cost function. When $a = 1$, the patient exhibits a constant marginal cost with cough duration and this is represented by a linear cost function. When $0 < a < 1$, the patient exhibits diminishing marginal cost with cough duration and this is represented by a concave cost function.

Prevalenc	Low	Norm	High
PNDS	0.22	0.34	0.44
Asthma	0.24	0.31	0.41
GERD	0.05	0.13	0.21

	Low	Norm	High
K	25	62.5	100
a	0.5	1	2

Sensitivity	Low	Norm	High
PNDS	0.97	0.985	1.0
Asthma	0.97	0.985	1.0
GERD	0.65	0.825	1.0

Specificity	Low	Norm	High
PNDS	0.67	0.73	0.79
Asthma	0.67	0.725	0.78
GERD	0.66	0.83	1.0

Figure 2: State Constants and Variables

4 Model Evaluation

By performing range sensitivity analysis, we can identify those parameters that vary the most within their range of values. It was identified that a was the most sensitive parameter followed by K, and the prevalence of $PNDS$. We performed sensitivity analyses on these three parameters to determine the extent to which variation of one or more of these parameters affecting the final decision.

One-Way Sensitivity Analysis A one-way sensitivity analysis was performed on a, K, and prevalence of $PNDS$, varying each of the parameters within their range of values as depicted in Figure 2 and holding the values of all other parameters at their nominal values. Among the three parameters, only the parameter a causes a shift to the final decision. As shown in Figure 3 the strategy Treat ALL is one of the cheapest when the value of a is low, however, when the value of a increases to above 1.74, the strategy Test All Then Treat becomes the cheapest of all. An intersection between Treat All and Test All Then Treat can also be observed from Figure 3 when the value of a is at 1.74.

Two-Way Sensitivity Analysis In this analysis, we vary the value of a from 0.5 to 2 and the value of K from 25 to 100, while holding all other variables at their nominal values. The results are presented in a graph with two regions of different colors each representing a different strategy. As depicted by Figure 4, the region with a greater surface area represents the strategy Treat All and the smaller region represents the strategy Test All Then Treat. The optimal strategy is Treat All when the values of a and K are low, and at higher values of a and K, the best choice is Test All Then Treat.

Three-Way Sensitivity Analysis The values of all the three most sensitive parameters, a, K, and prevalence of $PNDS$ were varied within their

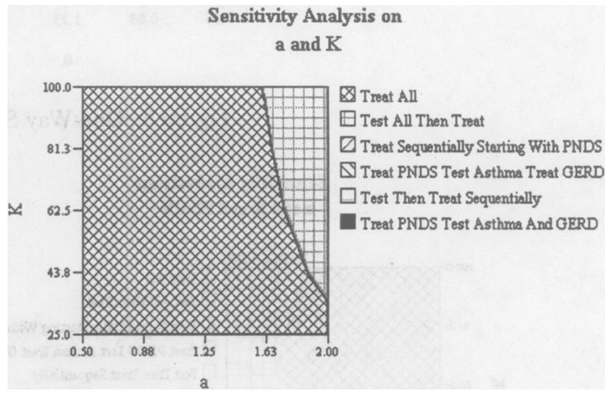


Figure 4: Two-Way Sensitivity Analysis on a and K

range of values as depicted in Figure 2. Figure 5 demonstrates how the two-way analysis of a and K change as the value of $PNDS$ varies from 0.22 to 0.44. As the prevalence of $PNDS$ increases, the strategy Test All Then Treat becomes less favorable, this is demonstrated in Figure 5, the area that represents Test All Then Treat is reduced when $PNDS$ increases from 0.22 to 0.44. It is also observed that at very low value of K and a, and very high value of $PNDS$, a new strategy Treat Sequentially Starting With PNDS becomes favorable. From Figure 5, we can see that a new region evolves when the value of $PNDS$ is at 0.44.

5 Discussion

From the above sensitivity analyses, we can deduced that the preferred strategies are Treat All, Test All Then Treat and Treat Sequentially Starting With PNDS. We can strengthen our deduction further by looking at Figure 6 which shows the *expected duration* and *expected direct cost* of each strategy. From Figure 6, it can be

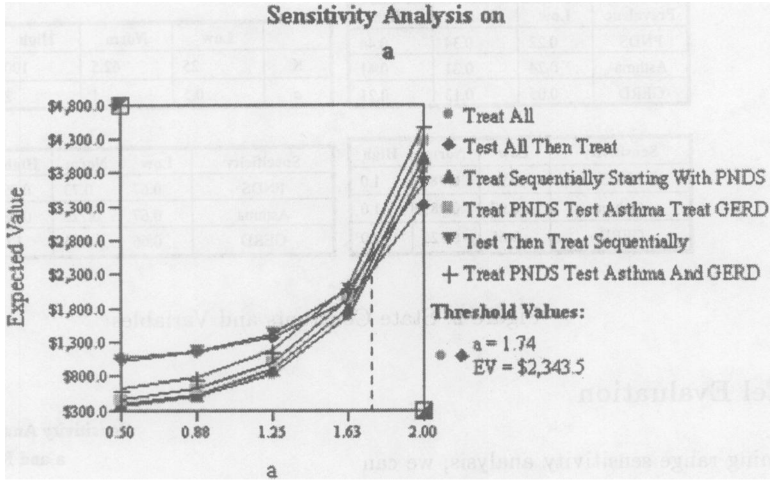


Figure 3: One-Way Sensitivity Analysis on a

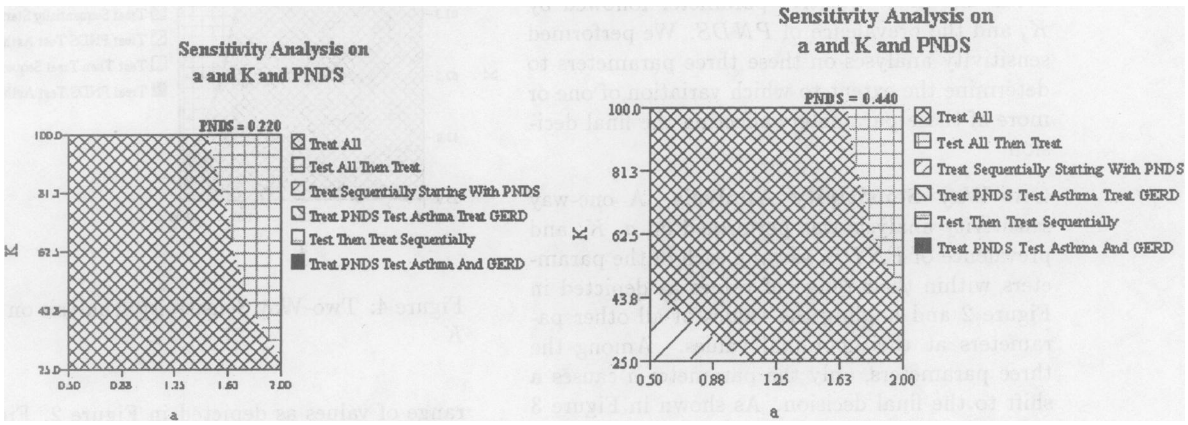


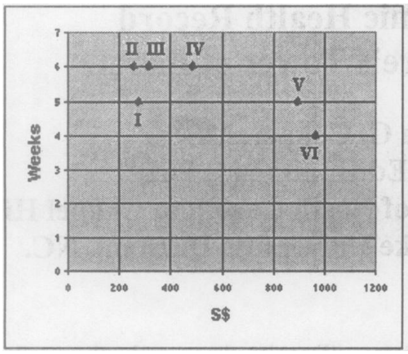
Figure 5: Three-Way Sensitivity Analysis on a, K and $PNDS$

observed that strategies III, IV, and V are dominated by the other three strategies, they can never be as efficient as strategies I, II, and VI under any circumstances, hence they can be omitted.

The strategy Test All Then Treat has the shortest treatment duration, however, it is also the most expensive strategy. On the other hand, the strategy Treat Sequentially Starting With PNDS is the cheapest, but with the longest treatment duration among those strategies that are under consideration. We also have a strategy Treat All that is slightly more expensive than Treat Sequentially Starting With PNDS, but has a shorter treatment duration. When compared to strategy Test All Then Treat, the strategy Treat All has a treatment duration that is one week longer, but at cost that is three times cheaper.

6 Conclusion

The outcome of our analysis demonstrates that three of the strategies dominate the rest of the strategies. Among these three dominating strategies, each of them exhibits optimality at different situations. The first dominating strategy, Test All Then Treat is the optimal strategy when the values of a and K are high, i.e. when the patient is very averse to prolonged coughing, and the opportunity cost of coughing for the first week is high. The next dominating strategy Treat Sequentially starting With PNDS is the best choice when the values of a and K are low, and the prevalence of $PNDS$ is high. The final optimum strategy, Treat All is the optimal choice when the values of a and K are moderately low, and the patient is very cost conscious. We can also observe that



I	Treat All	S$273	US$157	5 Weeks
II	Treat Sequentially	S$260	US$149	6 Weeks
III	Treat PNDS Test Asthma Treat GERD	S$319	US$184	6 Weeks
IV	Treat PNDS Test Asthma & GERD	S$487	US$280	6 Weeks
V	Test Then Treat Sequentially	S$897	US$516	5 Weeks
VI	Test All Then Treat	S$967	US$556	4 Weeks

Figure 6: Duration Vs Direct Cost

direct cost is objective; every patient managed by the same strategy will incur the same *direct cost*. On the other hand, *indirect cost* is subjective and patient centered; patients who underwent the same management strategy will not necessary incur the same *indirect cost*. Hence, in order to be cost effective in managing patients with chronic unexplained cough, the values of a, K and prevalence of $PNDS$, are some important parameters that require careful consideration. We hope that this model can be further refined and be used by practitioners.

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