Fuzzy Approach of Group Sequential Test for Binomial Case

Sevil Bacanlı *, Duygu Icen †, Salih Emri ‡

Abstract

The aim of this study is to present the fuzzy statistics into group sequential test when response variable has binomial case. Confidence intervals for fuzzy parameter estimation in group sequential test procedure is applied to construct the related fuzzy test statistic with the help of Buckley's approach with r-cuts. Afterwards, this present study is completed with a numerical application to real data. Finally it is concluded that the fuzzy approach is also applicable for group sequential tests when response variable has binomial case.

Keywords: Group sequential test, fuzzy statistics, asthma prevalence, Turkey

2000 AMS Classification: 62L05, 62L86

1 Introduction

One of the most important problems in medicine is the uncertainty between patients and medical relations. These relations are considered as inexact medical entities [2,3]. According to fuzzy set theory suggested by Zadeh [35], inexact medical entities can be defined as fuzzy sets. Theory of fuzzy sets is widely used for solving problems in which parameter or quantities cannot be expressed precisely. Buckley [6,7,8] introduced an approach that uses a set of confidence intervals. Furthermore, fuzzy sets present a number of powerful reasoning methods that can handle approximate inferences for medical data [9,19]. Several authors have proposed fuzzy approaches for medical researches. Reis [26] proposed a fuzzy expert model. This model could be used as a teaching or training tool that helps midwives, residents and medical students to identify and evaluate clinical risk factors. Duarte [11] tested a model to select patients for myocardial perfusion scintigraphy (MPS) based on fuzzy sets. Zolnoori [33,34] developed a fuzzy expert system for prediction of fatal asthma and evaluation of the level in asthma exacerbation.

Group sequential tests are not only used in clinical trials but also in medical studies due to their ethical, economical and administrative benefits. There is an extensive literature on group sequential tests and their application in clinical trials: an excellent summary is provided in Jennison and Turmbull [15]. As for medical studies, Pasternak and Shoe [23] demonstrated that the group sequential test had generally higher efficiency in a cohort study. Satagoban et al. [29] explain the use of a two stage group sequential test for gene-disease association studies. Aplenc et al. [4] give a description of group sequential test for molecular epidemiology study.

*Hacettepe University, Department of Statistics, 06800, Ankara, Turkey. Email: (S.Bacanlı) sevil@hacettepe.edu.tr

†Hacettepe University, Department of Statistics, 06800, Ankara, Turkey. Email: duyguicn@hacettepe.edu.tr

‡Hacettepe University, Department of Chest Diseases, 06100, Ankara, Turkey. Email: semri.editor@gmail.com

Group sequential tests have been applied to the normal, Binomial, inverse Gaussian and survival response variables [15,5]. Various group sequential test procedures have been suggested to analyze accumulated data in the literature [15]. Originally they were defined on the basis of a normalized Z statistic [24], or partial sum statistic [21,32]. Later, Kim and DeMets [16], Lan and DeMets [18], Pampallona and Anastasios [22], Chang, Hwang and Shih [10] proposed their designs based on error spending functions. Any of these procedures can have the overall type I (α) and type II (β) error while providing an opportunity for early stopping critical values [28].

Asthma is a chronic inflammatory disorder of the respiratory tract characterized by the infiltration of inflammatory cells, including mast cells, eosinophils, and lymphocytes [13,14,27]. It is a major cause of disability, utilization of health resource and poor quality of life around the world. In addition, asthma is the most common chronic disease among children and young adults. It causes considerable health care costs and loss of work productivity [31].

There is an epidemic of asthma affecting approximately 4% to 5% of people in developed countries. In United States, 20.1 million individuals are affected due to asthma and 6.3 million of them are children [1,30]. Emri [13] researched asthma prevalence in five urban regions in Turkey. It is found that the asthma prevalence 6.6%. After that, Kurt [17] evaluated the prevalence of risk factors for asthma and allergic diseases in Turkey.

In this study, it is indicated that group sequential test with $\alpha^*(t)$ functions for binomial response is applied to asthma data under the light of fuzzy approach. In many cases of real life, most of the data are approximately known. In addition to this, effects of measurement errors or unrecognized interactions are inevitable in every field of science. That is why, we use Buckley's fuzzy approach for estimating the asthma prevalence. Subsequently, fuzzy approach for group sequential test is applied to asthma prevalence in five Turkish urban regions. More information is used in the process of estimation and hypothesis testing with Buckley's approach than classical approach.

This paper is organized as follows; The definitions of fuzzy sets, triangular shaped fuzzy numbers, r-cut of triangular shaped fuzzy number and fuzzy probability are explained Section 2.1. Later, Buckley's approach for hypothesis testing is briefly reviewed in Section 2.2. Group sequential test based on $\alpha^*(t)$ spending functions and the adaptation of group sequential test according to Buckley's approach for a binomial case are given in Section 2.3. An illustrative example of the application of the fuzzy group sequential test to real asthma data from five Turkish urban regions is given in Section 3. Finally, concluding remarks are summarized in Section 4.

2 Theory and Methods

2.1 Fuzzy Sets and Triangular Shaped Fuzzy Numbers

A class of objects whose boundaries are not sharply defined is called as a fuzzy set. If $X = \{x\}$ denote a collection of objects, a fuzzy set $\widetilde{N}$ in X is a set of ordered pairs $\widetilde{N} = \{x, \mu_{\widetilde{N}}(x)\}, x \in X$ where $\mu_{\widetilde{N}}$ is the grade of membership of x in $\widetilde{N}$, $\mu_{\widetilde{N}}(x) : X \to M$ is a function from X to membership space M and produces values in $[0, 1]$ for all x. Hence the degree of membership of x in $\widetilde{N}$ is represented by $\mu_{\widetilde{N}}(x)$ which is a function having values between 0 and 1 [12].

The r-cuts of a fuzzy number, slices through a fuzzy number, is a non-fuzzy set defined as $\widetilde{N}(r) = \{x \in R, \mu_{\widetilde{N}}(x) \geq r\}$. Hence r-cut of a triangular shaped fuzzy number can be shown as $\widetilde{N}(r) = [N^L(r), N^U(r)]$, where $N^L(r)$ is the minimum value and $N^U(r)$ is the maximum value of the r-cut [12].

2.2 Hypothesis Testing using Buckley's Approach with r-cuts

One of the primary purposes of this statistical inference is to test the hypothesis. The problem of testing a hypothesis may be about the decision, since the decisions have to be made about the truth of two propositions, the null hypothesis H_0 and the alternative H_1. Furthermore, in traditional statistics, all parameters of the mathematical model should be very well defined. Sometimes these assumptions may appear too rigid for the real-life problems, especially dealing with imprecise requirements in medical studies. To lessen this rigidity, fuzzy methods are incorporated into statistics. In this section, Buckley's [6,7,8] approach for hypothesis testing that the parameter of crisp binomial distribution is defined as a triangular fuzzy number is summarized.

Let P be the probability of a success so that $Q = 1 - P$ is the probability of a failure. It is obtained x successes in a random sample size n so $p = x/n$ is the point estimate of P. The classical hypothesis for binomial distribution is defined as $H_0 : P = P_0$ versus $H_1 : P \neq P_0$. The test statistic

$$Z_0 = \frac{p - P_0}{\sqrt{P_0\, Q_0/n}} \tag{2.1}$$

is approximately standard normal distribution if n is sufficiently large. Then, decision rule is: (1) reject H_0 if $Z_0 \geq z_{\alpha/2}$ or $Z_0 \leq -z_{\alpha/2}$; and (2) do not reject H_0 when $-z_{\alpha/2} \leq Z_0 \leq z_{\alpha/2}$. In the above decision rule $\pm z_{\alpha/2}$ are called critical values (CV) for the test. In the decision rule $z_{\alpha/2}$ is the z value so that probability of random variable having the $N(0,1)$ probability density, exceeding z is $\alpha/2$.

It is known that $(p-P)/\sqrt{PQ/n}$ is approximately $N(0,1)$ if n is sufficiently large. At that case

$$P\left(p - z_{\alpha/2}\sqrt{p\, q/n} \leq\ P\ \leq p + z_{\alpha/2}\sqrt{p\, q/n}\right) = (1-\alpha). \tag{2.2}$$

This interval can be arranged according to the method proposed by Buckley [7,8] with substituting $(1-\alpha)100\%$ confidence interval for all $0.01 \leq \alpha \leq 1$. So equation (2.2) is defined by the following equation,

$$[p^L(\alpha), p^U(\alpha)] = [p - z_{\alpha/2}\sqrt{pq/n}, p + z_{\alpha/2}\sqrt{pq/n}]. \tag{2.3}$$

By placing these confidence intervals one after the other, a triangular shaped fuzzy number $\widetilde{p}$ whose r-cuts are the confidence intervals as

$$\widetilde{p}[r] = [p^L(r), p^U(r)], \tag{2.4}$$

is given

$$\widetilde{p}[r] = [p - z_{r/2}\sqrt{pq/n}, p + z_{r/2}\sqrt{pq/n}] \tag{2.5}$$

for $0.01 \leq r \leq 1$. Hence the fuzzy parameter estimation of P as triangular shaped fuzzy number is obtained.

By substituting equation (2.5) for p into equation (2.1), r-cuts of fuzzy test statistic are obtained as

$$\begin{aligned} \widetilde{Z}[r] &= \frac{\widetilde{p}[r] - P_0}{\sqrt{P_0 Q_0/n}} \\ &= \left[Z_0 - z_{r/2}\sqrt{\frac{pq}{P_0 Q_0}}, Z_0 + z_{r/2}\sqrt{\frac{pq}{P_0 Q_0}}\right]. \end{aligned} \tag{2.6}$$

Each r-cut is put one over the other, in order to get a triangular fuzzy test statistic $\widetilde{Z}[r]$. Calculations are performed by r-cuts and interval arithmetic. Since test statistic is fuzzy, the critical values $\widetilde{CV}_i, i = 1, 2$, which are given with equation (2.7) and equation (2.8), will also be fuzzy. Let $\widetilde{CV}_1$ correspond to $-z_{\gamma/2}$; and let $\widetilde{CV}_2$ go with $z_{\gamma/2}$, in this way it is possible to write $\widetilde{CV}_1 = -\widetilde{CV}_2$.

$$\widetilde{CV}_2[r] = \left[z_{\alpha/2} - z_{r/2}\sqrt{\frac{p\,q}{P_0Q_0}}; z_{\alpha/2} + z_{r/2}\sqrt{\frac{p\,q}{P_0Q_0}} \right] \tag{2.7}$$

$$\widetilde{CV}_1[r] = \left[-z_{\alpha/2} - z_{r/2}\sqrt{\frac{p\,q}{P_0Q_0}}; -z_{\alpha/2} + z_{r/2}\sqrt{\frac{p\,q}{P_0Q_0}} \right] \tag{2.8}$$

Both $\widetilde{CV}_1$ and $\widetilde{CV}_2$ are triangular shaped fuzzy numbers. In addition to this, r ranges in the interval $[0.01, 1]$. Final decision rule depends on the positions of fuzzy critical values: (1) $\widetilde{CV}_2 < \widetilde{Z}$ reject H_0; (2) $\widetilde{CV}_1 < \widetilde{Z} \approx \widetilde{CV}_2$ no decision; (3) $\widetilde{CV}_1 < \widetilde{Z} < \widetilde{CV}_2$ do not reject H_0; (4) $\widetilde{CV}_1 \approx \widetilde{Z} < \widetilde{CV}_2$ no decision; (5) $\widetilde{Z} < \widetilde{CV}_1$ reject H_0 [6,7,8].

2.3 Group sequential test for a binomial case using Buckley's approach with r-cuts

Several authors have proposed group sequential tests according to the significance levels:(i) constant levels for Pocock [24] and (ii) slowly increasing levels for O'Brien and Flemmnig [21]. These tests can be used when the group sizes are equal. In 1980s, first generation methods were generalized by Kim and DeMets [16] with the $\alpha^*(t)$ which allows one to characterize the rate at which the α risk is spent. The time t is the so-called information fraction in which the information is observed at a given time and divided by the total information which is at the end of the study. For example: $t = n/N$ can be given as a quantitative endpoint which represents the division of the number of patients at a given time with the number of patients at the end of the study [30]. In this group sequential test, it is determined that a discrete sequential critical value $(c_1, c_2, ..., c_K)$ is constructed by choosing positive constants $\alpha_1, ..., \alpha_K$ so $\sum \alpha_i = \alpha$, $P(Z_1 \geq c_1) = \alpha_1$ and $i = 2, ..., K$, $P(Z_i \geq c_i, Z_j \leq c_j, j = 1, ..., i-1) = \alpha_i$ [18]. Several examples of functions are existed in the literature. In this study $\alpha_i^*(t)$s $(i = 1, 2, ..., 5)$ are used as follows;

1. $\alpha_1^*(t) = 2[1 - \varphi(Z_{1-\alpha/2}/\sqrt{t})]$ $\quad 0 \leq t \leq 1$
2. $\alpha_2^*(t) = \alpha[ln[1 + (e-1)t]]$ $\quad 0 \leq t \leq 1$
3. $\alpha_3^*(t) = \alpha\, t$ $\quad 0 \leq t \leq 1$
4. $\alpha_4^*(t) = \alpha\, t^{3/2}$ $\quad 0 \leq t \leq 1$
5. $\alpha_5^*(t) = \alpha\, t^2$ $\quad 0 \leq t \leq 1.$

When the group sizes are equal, it generates $\alpha_1^*(t)$, discrete c_k approximate to those of O'Brien and Fleming [21] and it generates $\alpha_2^*(t)$, c_k approximate to those of Pocock [24]. Reboussin et al. [25] introduced a program to perform computations related to the design and analysis of group sequential clinical tests using [16] spending functions. The program and detailed information are publicly available at `http://www.biostat.wisc.edu/landemets`[25].

Firstly, it is considered that the primary outcome of group sequential test is binary. A sequence of independent Bernoulli random variables $X_1, X_2, \ldots$ is taken into consideration with $P(X_i = 1) = P$ and $P(X_i = 0) = 1 - P$. If data are divided with the total numbers of observations $n_1, n_2, \ldots, n_K$ as group sequentially in analysis 1 to K, the usual estimate of P in analysis k is given as such:

$$p^{(k)} = \frac{1}{n_k}\sum_{i=1}^{n_k} X_i \tag{2.9}$$

which has variance $P(1-P)/n_k$ and expectation P. The standardized statistics which are given in equation (2.10), may be used for constructing a two sided test

$$Z_k = (p^{(k)} - P_0)\sqrt{I_k} \quad , k = 1, \ldots, K \tag{2.10}$$

in which $I_k = n_k/\{P_0(1-P_0)\}$. The test statistic Z_k, is compared with c_k as follows; **1.** After group $k = 1, 2, \ldots, K-1$, if $Z_k \geq c_k$ stop reject H_0, otherwise continue to $k+1$. **2.** After group K, if $Z_K \geq c_K$ stop reject H_0, otherwise accept H_0.

After the classical approach of group sequential test is reviewed, let us proceed to fuzzy approach in which the estimate of P is a triangular shaped fuzzy number and its r-cuts are given with equation (2.5).

In order to perform $H_0 : P = P_0$ versus $H_1 : P > P_0$, equation (2.9) is calculated in every step of group sequential test. The uncertainty of this parameter is taken into account during the process and is taken as triangular shaped fuzzy number. Hence for each stage of the process in group sequential tests, fuzzy parameter estimation of $p^{(k)}$ is calculated with equation (2.11) for $0.01 \leq r \leq 1$.

$$\widetilde{p}^{(k)}[r] = \left[p^{(k)} - z_{r/2}\sqrt{\frac{p^{(k)}\ q^{(k)}}{n_k}};\ p^{(k)} + z_{r/2}\sqrt{\frac{p^{(k)}\ q^{(k)}}{n_k}}\right] \tag{2.11}$$

Better results can be attained with fuzzy approach which considers all confidence intervals as $(\widetilde{p}^{(k)}[r], 0.01 \leq r \leq 1)$ for unknown parameter $p^{(k)}$ in the process of group sequential test rather than classical approach for unknown parameter $p^{(k)}$. Calculations are performed with interval arithmetic. Substituting r-cuts of $\widetilde{p}^{(k)}$ into the equation (2.10) makes it possible to simplify by using interval arithmetic to produce $\widetilde{Z}_k[r]$ which is given below

(2.12)

$$\begin{aligned}\widetilde{Z}_k[r] &= (\widetilde{p}^{(k)}[r] - P_0)\sqrt{I_k} \\ &= [Z_k - z_{r/2}\sqrt{\tfrac{p^{(k)}q^{(k)}}{P_0Q_0}}; Z_k + z_{r/2}\sqrt{\tfrac{p^{(k)}q^{(k)}}{P_0Q_0}}], \quad \text{for} \quad k = 1, 2, \ldots, K.\end{aligned}$$

Each r-cut is placed one after the other in order to get a fuzzy test statistic $\widetilde{Z}_k[r]$ at each step of group sequential test. Since the test statistic is fuzzy, the critical values will also, be fuzzy. Thus, substituting c_k for $\alpha_i^*(t)$ functions for z_α continues and then, each r-cut of fuzzy critical value $\widetilde{CV}^*_{(i)k}[r] = [cv_{1ik}(r); cv_{2ik}(r)]$ can be evaluated with given calculations below

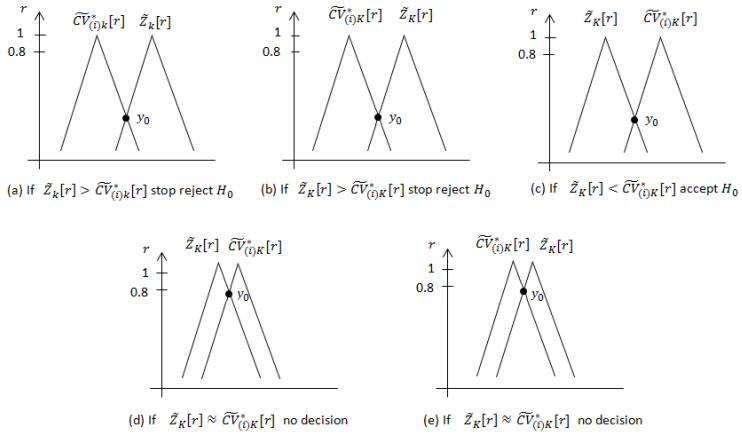
$$P\left(Z_k + z_{r/2}\sqrt{\frac{p^{(k)}q^{(k)}}{P_0\ Q_0}} \geq cv_{2ik}(r)\right) = \alpha \tag{2.13}$$

Therefore, fuzzy critical values of group sequential tests for binomial case can be defined as

$$\widetilde{CV}^*_{(i)k}[r] = \left[c_k - z_{r/2}\sqrt{\frac{p^{(k)}\ q^{(k)}}{P_0\ Q_0}}; c_k + z_{r/2}\sqrt{\frac{p^{(k)}\ q^{(k)}}{P_0\ Q_0}}\right] \tag{2.14}$$

Therefore, the fuzzy test process is as follows; **1.** After group $k = 1, 2, \ldots, K-1$, if $\widetilde{Z}_k[r] > \widetilde{CV}^*_{(i)k}[r]$ stop reject H_0, otherwise continue to $k+1$. **2.** After group

Figure 1: Decision criteria of r-cuts approach in group sequential test for binomial case



K, if $\widetilde{Z}_K[r] > \widetilde{CV}^*_{(i)K}[r]$ stop reject H_0, if $\widetilde{Z}_K[r] < \widetilde{CV}^*_{(i)K}[r]$ accept H_0, if $\widetilde{Z}_K[r] \approx \widetilde{CV}^*_{(i)K}[r]$ no decision.

These situations are detailed in Figure 1. As a result final decision depends on the relationship between $\widetilde{Z}_k[r]$ and $\widetilde{CV}^*_{(i)k}[r]$ for $k = 1, 2, .., K$: (a) $\widetilde{Z}_k[r] > \widetilde{CV}^*_{(i)k}[r]$ reject H_0 (Fig.1-a), (b) $\widetilde{Z}_K[r] > \widetilde{CV}^*_{(i)K}[r]$ stop reject H_0 (Fig.1-b), (c) $\widetilde{Z}_K[r] < \widetilde{CV}^*_{(i)K}[r]$ accept H_0 (Fig.1-c), (d) $\widetilde{Z}_K[r] \approx \widetilde{CV}^*_{(i)K}[r]$ no decision (Fig.1-d,e).

In Figure 1, height of the intersection between two triangular shaped fuzzy number is given as y_0. Buckley and some of the works that uses Buckley's approach state that if $y_0 = 0.8$ than it is impossible to compare these two numbers [6,7,8]. Hence it is taken into account that $y_0 = 0.8$ value for the fuzzy test process decides how much $\widetilde{Z}_k[r]$ is bigger than or less than $\widetilde{CV}^*_{(i)k}[r]$ for $k = 1, 2, .., K$. In some cases it is possible to calculate $\widetilde{Z}_k[r] \approx \widetilde{CV}^*_{(i)k}[r]$ (Fig.1-d,e) for $k = 1, 2, .., K$, so the final decision is *"no decision"* on H_0. That is the result of the fuzzy numbers that incorporate all the uncertainty in confidence intervals [6,7,8]. It is also possible to describe the fuzzy hypothesis testing procedure in more detailed and realistic way when the value of the test statistic is very close to the quantile of the test statistic.

Within the framework of the information given in Section 2.2, group sequential test is modified based on α-spending function for binomial case according to Buckley's approach. In Buckley's approach, fuzzy test statistic is obtained by using more than one confidence interval as the r-cut of triangular shaped fuzzy number. Thus; in this hypothesis testing procedure, group sequential test is done by taking into consideration more than one r value instead of just one value ($r = 1$) and that is the advantage of Buckley's fuzzy approach. Therefore, in this study, it is intended to demonstrate how to use fuzzy approach proposed by Buckley, in group sequential test based on α-spending function for binomial case.

3 An illustrative example

In this section, the use of fuzzy approach to medical data in group sequential test based on $\alpha_i^*(t)$ functions will be described. The medical data of this study is taken from a representative sample of adult population of Turkey which takes parts in the first national fluid and food consumption survey. It is also indicated that, applied survey is intended to reveal the general health status of a representative Turkish population

[13]. Emri at al. [13] researched asthma prevalence in five urban centers in Turkey. In Table 1, the prevalence of asthma is shown for five urban regions. Asthma prevelance is 5.6% in Kütahya, 9% in Eskisehir, 5.2% in Mersin, 8.7% in Aksaray and 4.3% in Sakarya. On the whole, one hundred and seven (6.6%) participants stated that they are diagnosed with asthma by a physician in Turkey.

Table 1: Prevalence of asthma cases by region (five urban regions, 2002)

	Kutahya	Eskisehir	Mersin	Aksaray	Sakarya	Total
n(%)	19(5.6)	32(9.0)	19(5.2)	26(8.7)	11(4.3)	107(6.6)
Total	337	357	365	300	255	1614

Traditional statistical analysis is based on crispness of data, random variable, point estimation and so on. However, in real life, it is known that there are many different situations in which the above mentioned concepts are imprecise. Moreover, effects of measurement errors or unrecognized interactions in the estimations of prevalence are inevitable [2,3]. In Buckley's approach, fuzzy asthma prevalence is obtained by using more than one confidence interval as the r-cut of triangular shaped fuzzy number. Thus, more information is used than in the classical approach.

The fuzzy estimations of asthma prevalence for each region are given in Table2. Calculations are performed within the scope of Maple 9 [20]. The fuzzy asthma prevalence for each region is estimated. For example, it is appropriate to say that the asthma prevalence for Kütahya is almost 5.6%, whose r-cuts are represented in Table2. Moreover, it is possible to see both lower (L) and upper (U) values of the estimated asthma prevalence for each region. Here, more information is used regarding not only one value but also all the confidence levels for the estimation of ashtma prevalence under the guidance of Buckley's approach. In more detail, the lower and upper values of estimated asthma prevalence are given such as $r = 0.01$, $r = 0.20$, $r = 0.40$, $r = 0.60$, $r = 0.80$ and lastly $r = 1$ for each region. In Table 2, it can be seen that, if r-cuts increase, lower and upper bounds get closer. If $r = 1$ is taken for each region, the classical results of asthma prevalence which are given in Table 1 is achieved. By estimating the fuzzy prevalence of asthma for each region, more information is used compared to the classical method. Besides, the measurement errors in calculation mistakes can be avoided by using these estimations.

Table 2: Fuzzy prevalence of asthma cases by region (five urban regions, 2002))

	p		$r = 0.01$	$r = 0.20$	$r = 0.40$	$r = 0.60$	$r = 0.80$	$r = 1.00$
Kutahya	5.6	L	5.580	5.584	5.590	5.593	5.597	**5.600**
		U	5.620	5.616	5.610	5.607	5.604	**5.600**
Eskisehir	9.0	L	8.975	8.980	8.987	8.992	8.996	**9.000**
		U	9.025	9.020	9.013	9.008	9.004	**9.000**
Mersin	5.2	L	5.181	5.186	5.191	5.195	5.198	**5.200**
		U	5.219	5.215	5.210	5.206	5.203	**5.200**
Aksaray	8.7	L	8.674	8.679	8.687	8.692	8.696	**8.700**
		U	8.728	8.728	8.714	8.708	8.704	**8.700**
Sakarya	4.3	L	4.278	4.284	4.289	4.294	4.297	**4.300**
		U	4.322	4.317	4.311	4.307	4.303	**4.300**
Total	6.6	L	6.589	6.592	6.595	6.597	6.598	**6.600**
		U	6.611	6.608	6.605	6.604	6.602	**6.600**

Classical group sequential test is applied for $H_0 : P = 0.06$ versus $H_1 : P > 0.06$ with significance level $\alpha = 0.05$, $K = 3$. Classical group sequential test results are given for different $\alpha_i^*(t)$ functions in Table 3. In this study, $\alpha_2^*(t)$ values are taken into account to test hypothesis at each stage for each region.

Table 3: Classical Group Sequential Test Results for different $\alpha_i^*(t)$ functions

		Stage		
Region		**k=1**	**k=2**	**k=3**
Kutahya	$t_i = \frac{n_i}{N_i}$	$200/337 = 0.594$	$270/337 = 0.801$	$337/337 = 1.000$
	$p_i = \frac{n_{\text{asthma}}}{n_i}$	$4/200 = 0.020$	$11/270 = 0.041$	$19/337 = 0.056$
	Z_i	-2.381	-1.335	-0.773
	$\alpha_1^*(t)$	2.292	1.195	1.739
	$\boldsymbol{\alpha_2^*(t)}$	**1.810**	**1.996**	**2.020**
	$\alpha_3^*(t)$	1.886	1.966	1.922
	$\alpha_4^*(t)$	1.988	1.950	1.836
	$\alpha_5^*(t)$	2.106	1.958	1.782
Eskisehir	$t_i = \frac{n_i}{N_i}$	$150/357 = 0.420$	$214/357 = 0.599$	$357/357 = 1.000$
	$p_i = \frac{n_{\text{asthma}}}{n_i}$	$6/150 = 0.040$	$15/214 = 0.070$	$32/357 = 0.089$
	Z_i	-1.031	0.616	1.796
	$\alpha_1^*(t)$	2.807	2.305	1.681
	$\boldsymbol{\alpha_2^*(t)}$	**1.924**	**2.074**	**1.950**
	$\alpha_3^*(t)$	2.033	2.093	1.857
	$\alpha_4^*(t)$	2.208	2.136	1.774
	$\alpha_5^*(t)$	2.373	2.201	1.727
Mersin	$t_i = \frac{n_i}{N_i}$	$76/365 = 0.208$	$220/365 = 0.603$	$365/365 = 1.000$
	$p_i = \frac{n_{\text{asthma}}}{n_i}$	$3/76 = 0.039$	$12/220 = 0.055$	$19/365 = 0.052$
	Z_i	-0.753	-0.344	-0.636
	$\alpha_1^*(t)$	4.139	2.271	1.680
	$\boldsymbol{\alpha_2^*(t)}$	**2.162**	**1.969**	**1.951**
	$\alpha_3^*(t)$	2.311	1.999	1.856
	$\alpha_4^*(t)$	2.594	2.048	1.770
	$\alpha_5^*(t)$	2.853	2.125	1.723
Aksaray	$t_i = \frac{n_i}{N_i}$	$100/300 = 0.333$	$200/300 = 0.667$	$300/300 = 1.000$
	$p_i = \frac{n_{\text{asthma}}}{n_i}$	$2/100 = 0.02$	$10/200 = 0.05$	$26/300 = 0.087$
	z_i	-1.853	-0.595	1.969
	$\alpha_1^*(t)$	3.200	2.141	1.695
	$\boldsymbol{\alpha_2^*(t)}$	**2.002**	**1.994**	**1.980**
	$\alpha_3^*(t)$	2.128	1.998	1.881
	$\alpha_4^*(t)$	2.341	2.019	1.792
	$\alpha_5^*(t)$	2.539	2.069	1.741
Sakarya	$t_i = \frac{n_i}{N_i}$	$119/255 = 0.467$	$194/255 = 0.761$	$255/255 = 1.000$
	$p_i = \frac{n_{\text{asthma}}}{n_i}$	$1/119 = 0.008$	$4/187 = 0.021$	$11/255 = 0.043$
	Z_i	-2.389	-2.228	-1.136
	$\alpha_1^*(t)$	2.642	1.989	1.722
	$\boldsymbol{\alpha_2^*(t)}$	**1.889**	**1.988**	**2.015**
	$\alpha_3^*(t)$	1.989	1.966	1.913
	$\alpha_4^*(t)$	2.150	1.957	1.822
	$\alpha_5^*(t)$	2.294	1.977	1.768

When the results for Kütahya are examined, it can be seen that asthma prevelance is 2% at stage 1 and test statistic is obtained as -2.381, this value is compared with the critical value $\alpha_2^*(t) = 1.81$. It takes us to the next step because $Z_1 = -2.381 < \alpha_2^*(t) = 1.81$. Then, in stage 2, it can bee seen that $Z_2 = -1.335 < \alpha_2^*(t) = 1.9964$, hence this leads us to next stage. In stage 3, $Z_3 = -0.773 < \alpha_2^*(t) = 2.020$ hence we stop and accept H_0.

Test statistic for Eskisehir is calculated as $Z_1 = -1.031$ in the first step and then comes the next step because $Z_1 = -1.031 < \alpha_2^*(t) = 1.9241$. In the second step, it is calculated that $Z_2 = 0.616 < \alpha_2^*(t) = 2.074$. Therefore it is proceeded with step 3. It is obtained that $Z_3 = 1.796 < \alpha_2^*(t) = 1.950$, thus we stop and accept H_0.

Test statistic for Mersin is calculated as $Z_1 = -0.753$ in the first stage, later, it leads us to the next step because $Z_1 = -0.753 < \alpha_2^*(t) = 2.162$. In the second step,

it is obtained that $Z_2 = -0.344 < \alpha_2^*(t) = 1.969$ hence this takes us to last step. Calculation is performed as such $Z_3 = -0.636 < \alpha_2^*(t) = 1.951$ in the third step so we stop and accept H_0.

Test statistic and critical value is obtained as $Z_1 = -1.853 < \alpha_2^*(t) = 2.002$ for Aksaray so it proceeds to second step. It is calculated as $Z_2 = -0.595 < \alpha_2^*(t) = 1.994$, therefore this takes us to step 3. It is obtained that $Z_3 = 1.969 < \alpha_2^*(t) = 1.9802$, thus we stop and accept H_0.

Test statistic for Sakarya is calculated as $Z_1 = -2.389$ in the first stage, then this leads us to the next step because $Z_1 = -2.389 < \alpha_2^*(t) = 1.889$. In the second step it is obtained that $Z_2 = -2.228 < \alpha_2^*(t) = 1.988$ hence it carries us to last step. It is calculated that $Z_3 = -1.136 < \alpha_2^*(t) = 2.015$ in the third step so we stop and accept H_0.

In Buckley's approach, fuzzy test statistic is obtained with using more than one confidence interval as the r-cut of triangular shaped fuzzy number. Thus, more information is used in hypothesis testing procedure. However, sample size is fixed in this approach. Fixed sample size is not beneficial in the medical studies in which data comes sequentially. For this purpose, it is illustrated in this section how to use fuzzy approach proposed by Buckley in group sequential test based on α-spending function for binomial case for the prevalence of asthma. Table 4-8 show the results of fuzzy group sequential test based on $\alpha_i^*(t)$ functions for asthma prevalence for Kütahya, Eskisehir, Mersin, Aksaray and Sakarya respectively by using fuzzy test statistics. In all regions, no matter which $\alpha_i^*(t)$ function has been used, (H_0) hypothesis has been accepted at the end of step 3. However, in Eskisehir and Aksaray regions, only of $\alpha_2^*(t)$ function is used, (H_0) hypothesis has been accepted at the end of step 3. If other functions are used, H_0 hypothesis has been rejected at the end of step 3. These tables give fuzzy estimations of asthma prevalence $\widetilde{p}_i[r]$, fuzzy test statistics $\widetilde{Z}_i[r]$ and fuzzy critical values $\widehat{\alpha}_i^*(t)$ with the help of equation (2.11), (2.12) and (2.14) for each urban regions in every stage of group sequential test. As a result, Table 4-8 indicate fuzzy group sequential test for different r-cuts ($r = 0.01, 0.20, 0.40, 0.60, 0.80, 1.00$).

Table 4: Fuzzy Group Sequential Test Results for different $\widetilde{\alpha}_i^*(t)$ functions for Kutahya.

Stage			$r = 0.01$	$r = 0.20$	$r = 0.40$	$r = 0.60$	$r = 0.80$	$r = 1.00$
$k = 1$ ($t_1 = 0.594$)	$\widetilde{p}_i[r]$	L	-0.005	0.001	0.004	0.005	0.019	**0.020**
		U	0.043	0.042	0.040	0.022	0.020	**0.020**
	$\widetilde{Z}_i[r]$	L	-3.911	-3.513	-3.106	-2.977	-2.412	**-2.381**
		U	-0.089	-1.912	-1.588	-2.103	-2.297	**-2.381**
	$\widetilde{\alpha}_1^*(t)$	L	0.765	1.531	1.784	1.973	2.156	**2.292**
		U	3.794	3.040	2.786	2.592	2.431	**2.292**
	$\widetilde{\alpha}_2^*(t)$	L	**0.291**	**0.932**	**1.302**	**1.645**	**1.713**	**1.810**
		U	**3.330**	**3.018**	**2.970**	**2.677**	**2.364**	**1.810**
	$\widetilde{\alpha}_3^*(t)$	L	0.364	1.119	1.383	1.566	1.728	**1.886**
		U	3.404	2.628	2.385	2.191	2.035	**1.886**
	$\widetilde{\alpha}_4^*(t)$	L	0.467	1.226	1.491	1.692	1.827	**1.988**
		U	3.491	2.738	2.478	2.299	2.136	**1.988**
	$\widetilde{\alpha}_5^*(t)$	L	0.579	1.345	1.595	1.786	1.959	**2.106**
		U	3.608	2.859	2.595	2.428	2.255	**2.106**
$k = 2$ ($t_2 = 0.801$)	$\widetilde{p}_i[r]$	L	0.005	0.012	0.022	0.031	0.039	**0.041**
		U	0.077	0.062	0.053	0.052	0.042	**0.041**
	$\widetilde{Z}_i[r]$	L	-3.552	-3.098	-2.365	-2.131	-1.612	**-1.335**
		U	0.653	0.077	-0.879	-0.978	-1.091	**-1.335**
	$\widetilde{\alpha}_1^*(t)$	L	-0.954	0.144	0.485	0.755	0.973	**1.195**
		U	3.319	2.259	1.886	1.622	1.391	**1.195**
	$\widetilde{\alpha}_2^*(t)$	L	**-0.084**	**0.715**	**1.210**	**1.764**	**1.874**	**1.996**
		U	**4.072**	**3.614**	**3.089**	**2.606**	**2.037**	**1.996**
	$\widetilde{\alpha}_3^*(t)$	L	-0.179	0.901	1.259	1.518	1.776	**1.966**
		U	4.069	2.996	2.658	2.359	2.154	**1.966**
	$\widetilde{\alpha}_4^*(t)$	L	-0.191	0.891	1.234	1.531	1.736	**1.950**
		U	4.073	2.997	2.647	2.383	2.159	**1.950**
	$\widetilde{\alpha}_5^*(t)$	L	-0.212	0.886	1.250	1.535	1.753	**1.958**
		U	4.061	3.016	2.652	2.401	2.156	**1.958**
$k = 3$ ($t_1 = 1.000$)	$\widetilde{p}_i[r]$	L	-0.003	0.021	0.042	0.050	0.052	**0.056**
		U	0.081	0.080	0.074	0.061	0.058	**0.056**
	$\widetilde{Z}_i[r]$	L	-3.192	-2.658	-1.889	-1.367	-0.978	**-0.773**
		U	1.591	1.356	0.017	-0.029	-0.589	**-0.773**
	$\widetilde{\alpha}_1^*(t)$	L	-0.778	0.486	0.935	1.225	1.461	**1.739**
		U	4.233	3.007	2.551	2.233	1.994	**1.739**
	$\widetilde{\alpha}_2^*(t)$	L	**-0.390**	**0.007**	**0.908**	**1.209**	**1.906**	**2.020**
		U	**4.540**	**3.968**	**3.307**	**3.0281**	**2.783**	**2.020**
	$\widetilde{\alpha}_3^*(t)$	L	-0.572	0.677	1.103	1.423	1.675	**1.922**
		U	4.402	3.145	2.711	2.444	2.147	**1.922**
	$\widetilde{\alpha}_4^*(t)$	L	-0.644	0.560	1.017	1.314	1.603	**1.836**
		U	4.315	3.020	2.708	2.334	2.075	**1.836**
	$\widetilde{\alpha}_5^*(t)$	L	-0.721	0.551	0.963	1.290	1.557	**1.782**
		U	4.276	3.050	2.593	2.296	2.104	**1.782**

Table 5: Fuzzy Group Sequential Test Results for different $\widetilde{\alpha}_i^*(t)$ functions for Eskisehir

Stage			$r = 0.01$	$r = 0.20$	$r = 0.40$	$r = 0.60$	$r = 0.80$	$r = 1.00$
	$\widetilde{p}_i[r]$	L	-0.001	0.019	0.027	0.032	0.036	**0.040**
		U	0.081	0.061	0.053	0.048	0.044	**0.040**
	$\widetilde{Z}_i[r]$	L	-3.064	-2.010	-1.685	-1.435	-1.226	**-1.031**
		U	0.986	-0.007	-0.349	-0.643	-0.832	**-1.031**
	$\widetilde{\alpha}_1^*(t)$	L	0.779	1.793	2.141	2.397	2.613	**2.807**
		U	4.827	3.804	3.451	3.204	2.997	**2.807**
$k = 1$	$\widetilde{\alpha}_2^*(t)$	L	**-1.116**	**0.901**	**1.262**	**1.515**	**1.731**	**1.924**
$t_1 = 0.420$		U	**3.949**	**2.940**	**2.588**	**2.326**	**2.107**	**1.924**
	$\widetilde{\alpha}_3^*(t)$	L	0.004	1.023	1.372	1.614	1.861	**2.033**
		U	4.053	3.039	2.704	2.443	2.232	**2.033**
	$\widetilde{\alpha}_4^*(t)$	L	0.175	1.225	1.542	1.789	2.014	**2.208**
		U	4.228	3.262	2.905	2.631	2.407	**2.208**
	$\widetilde{\alpha}_5^*(t)$	L	0.344	1.372	1.711	1.958	2.170	**2.373**
		U	4.393	3.449	3.043	2.787	2.580	**2.373**
	$\widetilde{p}_i[r]$	L	0.026	0.047	0.055	0.060	0.066	**0.070**
		U	0.114	0.092	0.085	0.087	0.074	**0.070**
	$\widetilde{Z}_i[r]$	L	-2.026	-0.712	-0.259	0.081	0.358	**0.616**
		U	3.236	1.954	1.497	1.135	0.858	**0.616**
	$\widetilde{\alpha}_1^*(t)$	L	-0.321	0.996	1.450	1.792	2.058	**2.305**
		U	4.927	3.615	3.145	2.839	2.573	**2.305**
$k = 2$	$\widetilde{\alpha}_2^*(t)$	L	**-0.563**	**0.769**	**1.208**	**1.530**	**1.805**	**2.074**
$t_2 = 0.599$		U	**4.690**	**3.368**	**2.939**	**2.612**	**2.311**	**2.074**
	$\widetilde{\alpha}_3^*(t)$	L	-0.549	0.758	1.228	1.560	1.830	**2.093**
		U	4.725	3.408	2.954	2.642	2.351	**2.093**
	$\widetilde{\alpha}_4^*(t)$	L	-0.501	0.816	1.255	1.587	1.883	**2.13**6
		U	4.758	3.461	3.001	2.675	2.404	**2.136**
	$\widetilde{\alpha}_5^*(t)$	L	-0.446	0.902	1.325	1.678	1.938	**2.201**
		U	4.817	3.505	3.071	2.734	2.448	**2.201**
	$\widetilde{p}_i[r]$	L	0.051	0.071	0.077	0.082	0.086	**0.089**
		U	0.27	0.108	0.102	0.097	0.094	**0.089**
	$\widetilde{Z}_i[r]$	L	-1.161	0.313	0.844	1.189	1.528	**1.796**
		U	4.736	3.245	2.754	2.398	2.104	**1.796**
	$\widetilde{\alpha}_1^*(t)$	L	-1.277	0.206	0.693	1.103	1.415	**1.681**
		U	4.649	3.144	2.630	2.280	1.973	**1.681**
$k = 3$	$\widetilde{\alpha}_2^*(t)$	L	**-1.008**	**0.467**	**1.015**	**1.355**	**1.695**	**1.950**
$t_3 = 1.000$		U	**4.897**	**3.438**	**2.918**	**2.550**	**2.238**	**1.950**
	$\widetilde{\alpha}_3^*(t)$	L	-1.100	0.394	0.908	1.247	1.565	**1.857**
		U	4.804	3.332	2.812	2.495	2.139	**1.857**
	$\widetilde{\alpha}_4^*(t)$	L	-1.178	0.298	0.835	1.186	1.418	**1.774**
		U	4.720	3.194	2.745	2.378	2.034	**1.774**
	$\widetilde{\alpha}_5^*(t)$	L	-1.231	0.246	0.772	1.149	1.428	**1.727**
		U	4.673	3.185	2.703	2.309	2.019	**1.727**

Table 6: Fuzzy Group Sequential Test Results for different $\widetilde{\alpha}_i^*(t)$ functions for Mersin

Stage			$r = 0.01$	$r = 0.20$	$r = 0.40$	$r = 0.60$	$r = 0.80$	$r = 1.00$
	$\widetilde{p}_i[r]$	L	-0.018	0.010	0.021	0.028	0.034	**0.039**
		U	0.097	0.068	0.058	0.051	0.045	**0.039**
	$\widetilde{Z}_i[r]$	L	-2.774	-1.676	-1.416	-1.172	-0.954	**-0.753**
		U	1.264	0.247	-0.097	-0.350	-0.583	**-0.753**
	$\widetilde{\alpha}_1^*(t)$	L	2.126	3.121	3.475	3.731	3.918	**4.139**
		U	6.153	5.152	4.766	4.547	4.332	**4.139**
$k = 1$	$\widetilde{\alpha}_2^*(t)$	L	**0.138**	**1.177**	**1.498**	**1.754**	**1.957**	**2.162**
$t_1 = 0.208$		U	**4.171**	**3.147**	**2.872**	**2.567**	**2.368**	**2.162**
	$\widetilde{\alpha}_3^*(t)$	L	0.294	1.306	1.651	1.919	2.110	**2.311**
		U	4.308	3.284	2.971	2.728	2.504	**2.311**
	$\widetilde{\alpha}_4^*(t)$	L	0.573	1.608	1.925	2.189	2.409	**2.594**
		U	4.602	3.595	3.237	3.002	2.815	**2.594**
	$\widetilde{\alpha}_5^*(t)$	L	0.836	1.872	2.225	2.436	2.660	**2.853**
		U	4.865	3.866	3.492	3.265	3.058	**2.853**
	$\widetilde{p}_i[r]$	L	0.015	0.035	0.042	0.047	0.051	**0.055**
		U	0.094	0.074	0.067	0.063	0.058	**0.055**
	$\widetilde{Z}_i[r]$	L	-2.686	-1.507	-1.108	-0.811	-0.572	**-0.344**
		U	1.993	0.850	0.420	0.132	-0.138	**-0.344**
	$\widetilde{\alpha}_1^*(t)$	L	-0.083	1.106	1.498	1.806	2.036	**2.271**
		U	4.611	3.412	3.030	2.731	2.516	**2.271**
$k = 2$	$\widetilde{\alpha}_2^*(t)$	L	**-0.382**	**0.802**	**1.223**	**1.474**	**1.730**	**1.969**
$t_2 = 0.603$		U	**4.310**	**3.136**	**2.733**	**2.435**	**2.198**	**1.969**
	$\widetilde{\alpha}_3^*(t)$	L	-0.361	0.813	1.225	1.537	1.769	**1.999**
		U	4.344	3.142	2.754	2.470	2.247	**1.999**
	$\widetilde{\alpha}_4^*(t)$	L	-0.302	0.891	1.265	1.577	1.814	**2.048**
		U	4.389	3.206	2.808	2.515	2.283	**2.048**
	$\widetilde{\alpha}_5^*(t)$	L	-0.237	0.962	1.342	1.664	1.901	**2.125**
		U	4.470	3.300	2.844	2.617	2.347	**2.125**
	$\widetilde{p}_i[r]$	L	0.022	0.037	0.043	0.046	0.049	**0.052**
		U	0.082	0.067	0.062	0.058	0.055	**0.052**
	$\widetilde{Z}_i[r]$	L	-2.374	-1.217	-0.817	-0.525	-0.282	**-0.636**
		U	2.224	1.081	0.681	0.398	0.173	**-0.636**
	$\widetilde{\alpha}_1^*(t)$	L	-0.621	0.524	0.954	1.243	1.467	**1.680**
		U	3.972	2.808	2.425	2.145	1.907	**1.680**
$k = 3$	$\widetilde{\alpha}_2^*(t)$	L	**-0.345**	**0.799**	**1.196**	**1.453**	**1.729**	**1.951**
$t_3 = 1.000$		U	**4.242**	**3.074**	**2.701**	**2.416**	**2.159**	**1.951**
	$\widetilde{\alpha}_3^*(t)$	L	-0.449	0.733	1.116	1.319	1.620	**1.856**
		U	4.148	3.003	2.606	2.321	2.101	**1.856**
	$\widetilde{\alpha}_4^*(t)$	L	-0.526	0.605	1.016	1.357	1.553	**1.770**
		U	4.026	2.936	2.534	2.230	2.011	**1.170**
	$\widetilde{\alpha}_5^*(t)$	L	-0.578	0.590	0.978	1.263	1.501	**1.723**
		U	4.015	2.884	2.468	2.197	1.964	**1.723**

Table 7: Fuzzy Group Sequential Test Results for different $\widetilde{\alpha}_i^*(t)$ functions for Aksaray

Stage			$r = 0.01$	$r = 0.20$	$r = 0.40$	$r = 0.60$	$r = 0.80$	$r = 1.00$
	$\widetilde{p}_i[r]$	L	-0.016	0.002	0.009	0.012	0.017	**0.020**
		U	0.056	0.038	0.032	0.027	0.024	**0.020**
	$\widetilde{Z}_i[r]$	L	-3.302	-2.573	-2.314	-2.150	-1.979	**-1.853**
		U	-0.415	-1.129	-1.388	-1.564	-1.709	**-1.853**
	$\widetilde{\alpha}_1^*(t)$	L	1.748	2.479	2.718	2.894	3.056	**3.200**
		U	4.646	3.914	3.675	3.492	3.351	**3.200**
$k = 1$	$\widetilde{\alpha}_2^*(t)$	L	**0.557**	**1.309**	**1.153**	**1.703**	**1.844**	**2.002**
$t_1 = 0.333$		U	**3.433**	**2.716**	**2.491**	**2.315**	**2.125**	**2.002**
	$\widetilde{\alpha}_3^*(t)$	L	0.697	1.421	1.688	1.829	1.984	**2.128**
		U	3.566	2.828	2.603	2.420	2.272	**2.128**
	$\widetilde{\alpha}_4^*(t)$	L	0.902	1.599	1.845	2.021	2.197	**2.341**
		U	3.758	3.055	2.752	2.633	2.492	**2.341**
	$\widetilde{\alpha}_5^*(t)$	L	1.101	1.818	2.057	2.226	2.395	**2.539**
		U	3.964	3.267	3.000	2.817	2.690	**2.539**
	$\widetilde{p}_i[r]$	L	0.011	0.030	0.037	0.042	0.046	**0.050**
		U	0.089	0.069	0.062	0.058	0.054	**0.050**
	$\widetilde{Z}_i[r]$	L	-2.856	-1.723	-1.345	-1.085	-0.825	**-0.595**
		U	1.643	0.509	0.131	-0.152	-0.412	**-0.595**
	$\widetilde{\alpha}_1^*(t)$	L	-0.116	1.033	1.381	1.678	1.949	**2.141**
		U	4.363	3.266	2.480	2.598	2.375	**2.141**
$k = 2$	$\widetilde{\alpha}_2^*(t)$	L	**-0.287**	**0.873**	**1.248**	**1.498**	**1.772**	**1.994**
$t_2 = 0.667$		U	**4.193**	**3.095**	**2.270**	**2.483**	**2.209**	**1.994**
	$\widetilde{\alpha}_3^*(t)$	L	-0.275	0.874	1.324	1.536	1.774	**1.998**
		U	4.234	3.073	2.698	2.448	2.261	**1.998**
	$\widetilde{\alpha}_4^*(t)$	L	-0.238	0.891	1.293	1.569	1.795	**2.019**
		U	4.218	3.138	2.774	2.485	2.184	**2.019**
	$\widetilde{\alpha}_5^*(t)$	L	-0.203	0.978	1.333	1.600	1.816	**2.069**
		U	4.304	3.200	2.819	2.565	2.311	**2.069**
	$\widetilde{p}_i[r]$	L	0.045	0.066	0.073	0.079	0.082	**0.087**
		U	0.129	0.108	0.100	0.095	0.091	**0.087**
	$\widetilde{Z}_i[r]$	L	-0.985	0.557	1.015	1.412	1.687	**1.969**
		U	4.847	3.442	2.908	2.542	2.236	**1.969**
	$\widetilde{\alpha}_1^*(t)$	L	-1.244	0.237	0.725	1.092	1.443	**1.695**
		U	4.558	3.153	2.619	2.298	1.932	**1.695**
$k = 3$	$\widetilde{\alpha}_2^*(t)$	L	**-0.959**	**0.492**	**0.980**	**1.347**	**1.698**	**1.980**
$t_3 = 1.000$		U	**4.874**	**3.423**	**2.965**	**2.568**	**2.263**	**1.980**
	$\widetilde{\alpha}_3^*(t)$	L	-1.008	0.465	0.940	1.278	1.569	**1.881**
		U	4.713	3.302	2.873	2.458	2.121	**1.881**
	$\widetilde{\alpha}_4^*(t)$	L	-1.132	0.334	0.853	1.158	1.509	**1.792**
		U	4.655	3.250	2.731	2.380	2.059	**1.792**
	$\widetilde{\alpha}_5^*(t)$	L	-1.168	0.282	0.863	1.122	1.458	**1.741**
		U	4.619	3.245	2.695	2.328	1.947	**1.741**

Table 8: Fuzzy Group Sequential Test Results for different $\widetilde{\alpha}_i^*(t)$ functions for Sakarya

Stage			$r=0.01$	$r=0.20$	$r=0.40$	$r=0.60$	$r=0.80$	$r=1.00$
	$\widetilde{p}_i[r]$	L	-0.013	-0.003	0.001	0.004	0.006	**0.008**
		U	0.029	0.019	0.015	0.012	0.010	**0.008**
	$\widetilde{Z}_i[r]$	L	-3.30	-2.820	-2.670	-2.579	-2.472	**-2.389**
		U	-1.480	-1.936	-2.075	-2.198	-2.284	**-2.389**
	$\widetilde{\alpha}_1^*(t)$	L	1.734	2.179	2.331	2.444	2.553	**2.642**
		U	3.556	3.122	2.949	2.829	2.715	**2.642**
$k=1$	$\widetilde{\alpha}_2^*(t)$	L	**0.970**	**1.433**	**1.591**	**1.728**	**1.788**	**1.889**
$t_1=0.467$		U	**2.807**	**2.332**	**2.185**	**2.076**	**1.995**	**1.889**
	$\widetilde{\alpha}_3^*(t)$	L	1.071	1.537	1.667	1.786	1.905	**1.989**
		U	2.892	2.447	2.252	2.160	2.062	**1.989**
	$\widetilde{\alpha}_4^*(t)$	L	1.222	1.682	1.854	1.959	2.056	**2.150**
		U	3.054	2.615	2.441	2.333	2.225	**2.150**
	$\widetilde{\alpha}_5^*(t)$	L	1.359	1.837	1.996	2.110	2.208	**2.294**
		U	3.209	2.758	2.586	2.593	2.374	**2.294**
	$\widetilde{p}_i[r]$	L	0.009	0.015	0.017	0.019	0.020	**0.021**
		U	0.033	0.027	0.025	0.024	0.023	**0.021**
	$\widetilde{Z}_i[r]$	L	-3.726	-2.982	-2.735	-2.545	-2.371	**-2.228**
		U	-0.739	-1.507	-1.759	-1.920	-2.086	**-2.228**
	$\widetilde{\alpha}_1^*(t)$	L	0.498	1.238	1.497	1.668	1.854	**1.989**
		U	3.472	2.744	2.477	2.284	2.131	**1.989**
$k=2$	$\widetilde{\alpha}_2^*(t)$	L	**0.487**	**1.241**	**1.496**	**1.682**	**1.839**	**1.988**
$t_2=0.761$		U	**3.475**	**2.706**	**2.477**	**2.258**	**2.131**	**1.988**
	$\widetilde{\alpha}_3^*(t)$	L	0.468	1.222	1.467	1.643	1.810	**1.966**
		U	3.435	2.695	2.441	2.245	2.114	**1.966**
	$\widetilde{\alpha}_4^*(t)$	L	0.459	1.192	1.460	1.642	1.794	**1.957**
		U	3.433	2.679	2.440	2.258	2.106	**1.957**
	$\widetilde{\alpha}_5^*(t)$	L	0.486	1.226	1.480	1.662	1.821	**1.977**
		U	3.453	2.758	2.489	2.256	2.119	**1.977**
	$\widetilde{p}_i[r]$	L	0.027	0.035	0.038	0.040	0.042	**0.043**
		U	0.060	0.051	0.049	0.046	0.045	**0.043**
	$\widetilde{Z}_i[r]$	L	-3.210	-2.176	-1.183	-1.153	-1.329	**-1.136**
		U	0.949	-0.118	-0.481	-0.734	-0.954	**-1.136**
	$\widetilde{\alpha}_1^*(t)$	L	-0.438	0.685	1.033	1.314	1.482	**1.722**
		U	3.795	2.762	2.369	2.156	1.920	**1.722**
$k=3$	$\widetilde{\alpha}_2^*(t)$	L	**-0.073**	**0.955**	**1.366**	**1.608**	**1.789**	**2.015**
$t_3=1.000$		U	**4.085**	**3.046**	**2.719**	**2.417**	**2.224**	**2.015**
	$\widetilde{\alpha}_3^*(t)$	L	-0.189	0.884	1.214	1.467	1.721	**1.913**
		U	3.973	2.923	2.570	2.310	2.122	**1.913**
	$\widetilde{\alpha}_4^*(t)$	L	-0.288	0.795	1.129	1.383	1.590	**1.822**
		U	3.872	2.846	2.489	2.235	2.028	**1.822**
	$\widetilde{\alpha}_5^*(t)$	L	-0.329	0.693	1.057	1.352	1.545	**1.768**
		U	3.863	2.807	2.398	2.170	1.977	**1.768**

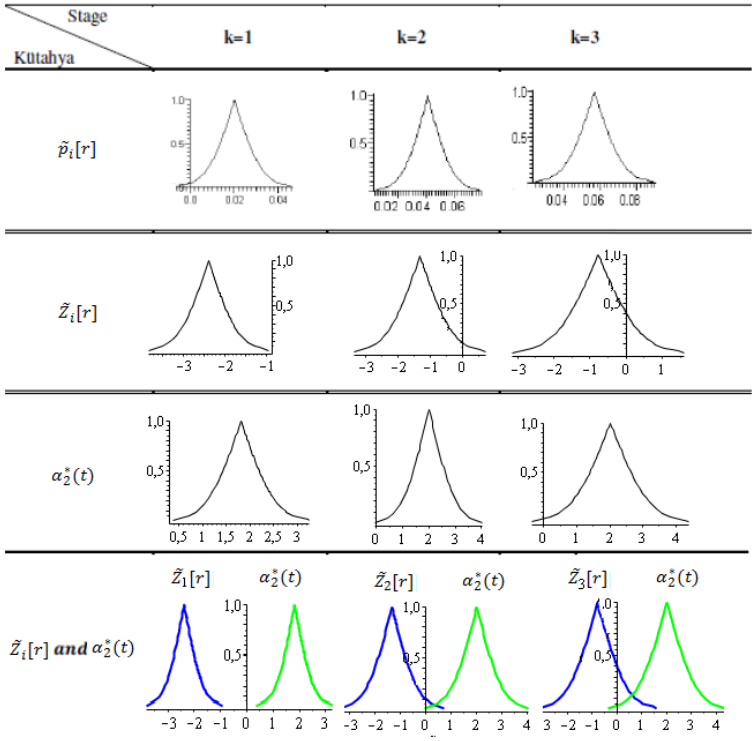
The results from $r=1$ are the same as the classical group sequential test. Thus, fuzzy group sequential test is carried out regarding more than one r value instead of just one ($r=1$), which is the advantage of fuzzy approach. Furthermore, researcher can test hypothesis in different levels. If researcher thinks that uncertainty level is high, then hypothesis can be tested at r=0.01. However, if s/he thinks uncertainty is low, then hypothesis can be tested at r=0.80. Besides, it is indicated that crisp values are obtained for group sequential test if $r=1$ is taken for each step. These values are given in Table 4-8.

For example, fuzzy asthma prevalence for Kütahya is calculated as $\widetilde{p}_1[r=0.20] = [0.001, 0.042]$ which gets narrower at $r=0.80$ as $\widetilde{p}_1[r=0.80] = [0.019, 0.020]$ at stage one. Furthermore, at $r=1.00$ it is obtained that $\widetilde{p}_1[r=1.00] = [0.020, 0.020]$

which is equal to the classical approach results for Kütahya in stage one. Besides, fuzzy test statistic is obtained as $\widetilde{Z}_1[0.20] = [-3.513, -1.912]$ and fuzzy critical value $\widetilde{CV}^*_{(2)1}[0.20] = [0.932, 3.018]$ for $r = 0.20$. It is obtained that $\widetilde{Z}_1[0.20] < \widetilde{CV}^*_{(2)1}[0.20]$, then with the framework of the test procedure, we continue to the next step. In the second step, it is calculated that $\widetilde{Z}_2[0.20] = [-3.098, 0.077] < \widetilde{CV}^*_{(2)2}[0.20] = [0.715, 3.614]$ this takes us to the last step. It is obtained that $\widetilde{Z}_3[0.20] = [-2.658, 1.356] < \widetilde{CV}^*_{(2)3}[0.20] = [0.007, 3.968]$ so we stop and accept H_0. Here H_0 is tested according to $r = 0.20$ level.

Fuzzy prevalence of ashthma ($\widetilde{p}_i[r]$), fuzzy test statistics ($\widetilde{Z}_i[r]$), fuzzy critical values are given in detail with Figure 2 for Kütahya in all r-cuts ($0.01 \leq r \leq 1$).

Figure 2: Membership functions of the values in Table 5 for Kutahya



In general, taking into consideration of all the r-cuts for each step with Figure 2, it is clear that $\widetilde{Z}_1 < \widetilde{CV}^*_{(2)1}$ for stage 1 ($k = 1$). In this case, it will proceed to the second stage ($k = 2$). In second stage $\widetilde{Z}_2 < \widetilde{CV}^*_{(2)2}$ hence this leads us to the last step ($k = 3$). When last stage is examined, it is obtained that $\widetilde{Z}_3 < \widetilde{CV}^*_{(2)3}$. It is possible to accept the null hypothesis ($H_0 : P = 0.06$ versus $H_1 : P > 0.06$) at the third stage for Kütahya by taking into consideration of the all uncertainty within the process of using r-cuts. Moreover, as the number of steps increases, fuzzy group sequential test statistic and fuzzy critical value get closer to each other. Hence, closer results to the real values can be achieved in the fuzzy group sequential tests rather than classical group sequential tests.

Same calculations are done for other regions. Therefore, fuzzy asthma prevalence ($\widetilde{p}_i[r]$), fuzzy test statistic ($\widetilde{Z}_i[r]$) and fuzzy critical values ($\widetilde{\alpha}^*_1(t)$,$\widetilde{\alpha}^*_2(t)$,$\widetilde{\alpha}^*_3(t)$,$\widetilde{\alpha}^*_4(t)$,$\widetilde{\alpha}^*_5(t)$) are obtained in each step for each region. These results can be seen in Table 5-8.

4 Conclusion

In this study, hypothesis testing is adapted by using r-cuts for group sequential test based on α-spending function under the guidance of the information given in Section 1. The advantage of r-cuts (fuzzy) approach is that, instead of generating and processing a single confidence interval, all the confidence intervals are calculated in the process of corresponding fuzzy test statistics. Therefore, in this study it is intended to show that this advantage is also valid for the process of group sequential test based on α-spending function. Thus, the advantages of fuzzy set theory is combined with the advantages of group sequential test. If $r = 1$ is taken in each step, fuzzy group sequential test turns into the classical group sequential test procedure.

Consequently, in this paper fuzzy set theory and Buckleys approach are used to solve problems of impreciseness arising in group sequential test for binomial case. Since, in the traditional statistical tests, the parameters are assumed to be precise values, difficulties arise when the parameters become imprecise, especially in the field of medicine. Hence, the vagueness of p usually comes from personal judgment, experiment or estimation, whose accuracy is limited by the experimental or observational errors. It is clear that Buckley's approach, which uses several confidence intervals rather than only one value for estimating and testing fuzzy parameter, is a well known tool. Additionally, group sequential test provide ethical, economical and administrative advantages. As a result, in this study the benefits of two methodologies are combined and it leads us to propose group sequential test for binomial case under the light of Buckley's approach with r-cuts. It is intended to illustrate that how the fuzzy group sequential test could be applied to real life by using asthma data for five urban regions in Turkey.

References

[1] Adams, B.K. and Cydulka, R.K. *Asthma evalution and management*, Emerg Med Clin N Am **21(2)**, 315-330, 2003.

[2] Adlassnig, K.P. *Fuzzy set theory in medical diagnosis*, Transactions on systems, Man,and Cybernetics, **16(2)**, 260-265, 1986.

[3] Adlassnig, K.P., Scheithauer, W., Grabner, G. *CADIAG-2/PANCREAS: An artificial intelligence system based on fuzzy set theory to diagnose pancreatic diseases*, Third International Conference on System Science in Health Care Health Systems Research, 396-399, 1984.

[4] Alpenc, R., Zhao, H., Rebbeck, T.R., Propert, K.J. *Group Sequential Methods and Sample Size Saving in Biomerker-Disease Association Studies*, Genetics **163(3)**, 1215-1219, 2003.

[5] Bacanlı, S., Demirhan, Y.P. *A group sequential test for inverse Gaussian mean*, Statistical Papers **49**, 377-386, 2008.

[6] Buckley, J.J. *Fuzzy Statistics* (Springer-Verlage, Hiedelberg:Germany), 2004.

[7] Buckley, J.J. *Fuzzy statistics:hypothesis testing*, Soft Comput **9**, 512-518, 2005.

[8] Buckley, J.J. *Fuzzy Probability and Statistics*. (Springer-Verlage, Hiedelberg: Germany), 2006.

[9] Castanho, M.J.P.,Barros, L.C.,Yamakami, A. and Venditei,L.L. *Fuzzy Receiver Operating Characteristic Curve: An Option to Evaluate Diagnostic Tests*, IEEE Transactions on Information Technology n Biomedicine **11(13)**, 244-250, 2007.

[10] Chang, M.N., Hwang, I.K, Shih, W.J. *Group sequential designs using both type I and type II error probability spending functions*, Commun. Statist.Part A Theory Methods **27(6)**, 1323-39, 1998.

[11] Duarte, P.S., Mastrocolla, L.E., Farsky, P.S., Sampaio, C.R.E.P.S., Tonelli, P.A., Barros, L.C., et al. *Selection of patients for myocardial perfusion scintigraphy based on fuzzy sets theory applied to clinical-epidemiological data and treadmill test results*, Brazilian Journal of Medical and Biological research **39(1)**,9-18, 2006.

[12] Dubois, D. and Prade, H. *Operations with fuzzy numbers*, Int J Syst Sci **9(6)**,613-626, 1978.

[13] Emri, S.,Turnagl, H.,Basoglu, S.,Bacanl, S.,Guven, G.S. and Aslan, D. *Asthma-like symptoms prevalence in five Turkish urban centers*, Allergol at Immunopathol **33(5)**,270-276, 2005.

[14] Green, R.H., Brighling, C.E., Pavord, I.D,, Wardlaw, A.J. *Management of asthma in adults:Current therapy and future directions*, Postgrad Med J **79**, 259-67, 2003.

[15] Jennison, C., Turnbull, B.W. *Group sequential methods with applications to clinical trials*,(Chapman and Hall,New York), 2000.

[16] Kim, K., DeMets, D.L. *Design and analysis of group sequential tests based on the type I error spending rate function*, Biometrika **74(1)**, 149-154, 1987.

[17] Kurt, E., Metintas, S., Basyigit, I., Bulut, I., Coskun, E., Dabak, S. et al. *Prevalence and riskfactors of allergies in Turkey (PARFAIT): results of multicenter cross-sectional study in adults*, Eur Respir J **33**, 724-733, 2009.

[18] Lan, K.K.G., DeMets, D.L. *Discrete sequential boundaries for clinical trials*, Biometrika **70(3)**, 659-663, 1983.

[19] Liang, R.L., Shiyong, L., Xuena, W., Yi, L., Vinay, M., Dorrelyn, P. and Deepak, K. *FM-test: a fuzzy-set-theory-based approach to differential gene expression data analysis, BMC.* Bioinformatics **4**,7, 2006.

[20] Maple 9, Waterloo Maple Inc.,Waterloo,Canada.

[21] O'Brien, P.C., Fleming, T.R. *A multiple testing procedure for clinical trials*, Biometrics **35(3)**,549556, 1979.

[22] Pampallona, S., Anastasios TA. *Group sequential desgns for one-sided and two-sided hypothesis testing with provision for early stopping in favor of the null hypothesis*, J Stat Plan Inference **42**, 19-35, 1994.

[23] Pasternak, B.S., Shore, R.E. *Group Sequential Methods for Cohort and Case-Control Studies*, J.Choronic Dis., **33(6)**, 365-373, 1980.

[24] Pocock, S.J. *Group sequential methods in the design and analysis of clinical trials.* Biometrika **64(2)**, 191199, 1977.

[25] Reboussin, D.M., DeMets, D.L., Kim, K., Lan, G.K.K. *Computations for Group Sequential Boundaries Using the Lan-DeMets spending function method*, Controlled Clinical Trials **21(3)**, 190-207, 2000.

[26] Reis, M.A.M., Ortega, N.R.S, Silveira, P.S.P. *Fuzzy expert system in the prediction of neonatal resuscitation*, Brazilian Journal of Medical and Biological Research **37(5)**, 755-764, 2004.

[27] Roy, R.S. *Asthma*, Southern Medical Journal **96(11)**, 1061-1067, 2003.

[28] Rudser, K.D., Emerson, S.S. *Implementing type I and type II error spending for two-sided group sequential designs*, Contemporary Clinical Trials **29(3)**, 351-358, 2008.

[29] Satagopan, J.M., Verbel, D.A., Venkatraman, E.S., Offit, K.E., Begg, C.B. *Two-Stage Designs for Gene-Disease Association Studies*, Biometrics **58**, 163-170, 2002.

[30] Sebille, V., Bellissant, E. *Sequential methods and group sequential designs for comparative clinical trials*, Fundamental and Clinical Pharmacology **17(5)**, 505-516, 2003.

[31] To, T., Stanojevic, S., Moores, G., Gershon, A.S., Bateman, E.D., Cruz, A.A., Boulet, L.P. *Global asthma prevelance in adults: findings from the cross-sectional world health survey*, BMC Public Health **12**, 204-211, 2012.

[32] Whitehead, J., Stratton, I. *Group sequential clinical trials with triangular continuation regions (corr:V39 p1137)*, Biometrics **39**, 227-36, 1983.

[33] Zolnoori, M., Zarandi, M.H.F., Moin, M. F*uzzy rule-base expert system for evaluation possibility of fatal asthma*, Journal of Health Informatics in Developing Countries **5(1)**, 171-184, 2010.

[34] Zolnoori, M., Zarandi, M.H.F., Moin, M. *Application of intelligent systems in asthma disease:designing a fuzzy rule-based system for evaluating level of asthma exacerbation*, J Med Syst **36(4)**, 2071-2083, 2012.

[35] Zadeh, L.A. *Fuzzy sets.* Information and control **8(3)**, 338-353, 1965.