

# Expert panel on cost analysis of atrial fibrillation

## *Atriyal fibrilasyon maliyet analizi için uzman paneli*

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### ABSTRACT

**Objective:** To estimate total cost of atrial fibrillation (AF) management concerning acute coronary syndrome, heart failure, stroke and drug related adverse events with respect to clinical practice and available guidelines.

**Methods:** This cost analysis study was based on identification of total costs related to management of acute coronary syndrome, heart failure, stroke and the drug related adverse events in patients with AF based on standardized questionnaire forms filled by experts according to their daily clinical practice and also to ACCF/AHA/ESC guidelines. Total cost included cost items related to treatment, healthcare resources utilization, and diagnostic test and consultations.

**Results:** The yearly cost of acute coronary syndrome per patient was 5.478.43 TL according to expert's view reflecting real clinical practice whereas it was 11.319.44 TL when calculation was based on recommendations in the guidelines. The average total cost of heart failure was 4.523.74 TL according to expert's view whereas it was 2.925.86 TL based on guidelines. The average total cost of stroke was 5.719.25 TL according to expert's view but 7.931.18 TL based on guidelines. Among drug related adverse events, only those related to cardiac adverse events were estimated to be higher according to expert view as compared to guideline recommendations (288.65 vs. 150.99 TL).

**Conclusions:** Reflecting the treatment algorithms in the management of AF and related adverse events, our findings seem to emphasize the extra burden on health economics posed by patients suffering from the uncontrolled disease. (*Anadolu Kardiyol Derg 2013; 13: 26-38*)

**Key words:** Atrial fibrillation, acute coronary syndrome, heart failure, stroke, adverse events, cost analysis

### ÖZET

**Amaç:** Atriyal fibrilasyon (AF) yönetimi toplam maliyetinin klinik uygulama ve kılavuzlar bazında hesaplanarak akut koroner sendrom, kalp yetersizliği, inme ve ilaca bağlı advers olaylar açısından maliyet verilerinin sağlanması.

**Yöntem:** Bu maliyet analiz çalışması, AF hastalarında akut koroner sendrom, kalp yetersizliği, inme ve ilaca bağlı advers olaylar bazında toplam maliyetin, kendi klinik pratikleri ve ACCF/AHA/ESC kılavuzlarında yer alan öneriler doğrultusunda araştırmacılar tarafından doldurulan standart anket formları aracılığı ile hesaplanması yolu ile yürütüldü. Toplam tıbbi maliyet hesabına dahil edilen maliyet kalemleri tedavi, sağlık kaynakları kullanımı, tanısal testler ve konsültasyon kalemleri olarak belirlendi.

**Bulgular:** Akut koroner sendrom için hesaplanan ortalama toplam maliyet, uzmanların günlük klinik pratiği yansıtan görüşlerine göre 5.478.43 TL iken kılavuzlar doğrultusunda 11.319.44 TL olarak hesaplandı. Kalp yetersizliği toplam maliyeti uzman görüşlerine göre 4.523.74 TL iken kılavuzlar doğrultusunda 2.925.86 TL olarak hesaplandı. İnme toplam maliyeti uzman görüşlerine göre 5.719.25 TL, kılavuzlara göre ise 7.931.18 TL olarak hesaplandı. İlaça bağlı advers olaylar içinde, yalnızca kardiyak advers olaylar için, uzman görüşleri doğrultusunda kılavuzlara göre daha yüksek maliyet tespit edildi (288.65 ve 150.99 TL).

**Sonuç:** Atriyal fibrilasyon ve ilgili advers olayların yönetiminde klinik pratikte kullanılan tedavi algoritmalarını yansıtan bulgularımız, hastalıkları kontrol altına alınamayan hastaların sağlık ekonomisine getirdiği fazladan maliyet yüküne işaret etmektedir.

(*Anadolu Kardiyol Derg 2013; 13: 26-38*)

**Anahtar kelimeler:** Atriyal fibrilasyon, akut koroner sendrom, kalp yetersizliği, inme, advers olaylar, maliyet analizi



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## Introduction

Characterized by uncoordinated atrial activation with consequent loss of atrial mechanical function, atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1-2% of the general population (1) associated with disturbed quality of life (2, 3), significant morbidity, increased risk of mortality and frequent medical intervention (4, 5). Being the most common arrhythmia in clinical practice, accounting for approximately one-third of hospitalizations for cardiac rhythm disturbances (5), the prevalence of AF was predicted to at least double by 2050 and indicated to be strongly dependent on age, increasing from 0.5% at 40-50 years, to 5-15% at 80 years (1). An estimated 2.3 million people in North America and 4.5 million people in the European Union have paroxysmal or persistent AF (6).

Owing to increasing prevalence, AF has been considered as an extremely costly public health problem, with hospitalizations as the primary cost driver (52%), followed by drugs (23%), consultations (9%), further investigations (8%), loss of work (6%), and paramedical procedures (2%) (5).

In the last 2 decades, there has been a 66% increase in emergency department visits/hospital admissions for AF due to a combination of factors including the aging of the population, a rising prevalence of chronic heart disease, and more frequent diagnosis through use of ambulatory monitoring devices (5, 7).

Globally, AF is an extremely expensive public health problem [approximately €3000 (approximately U.S. \$3600) annually per patient]; the total cost burden approaches €13.5 billion (approximately U.S. \$15.7 billion) in the European Union (5, 8).

Owing to its highly pleiomorphic and dynamic nature that spans the spectrum from a primary electrical disturbance to an arrhythmia that develops in response to electrical, structural, and functional remodeling in response to a diverse number of cardiovascular insults or stressors (9), AF in older persons generally does not occur in isolation but is frequently accompanied by other age-related cardiovascular conditions (hypertension, coronary artery disease, diabetes, and chronic heart failure (CHF)), pulmonary diseases and chronic or even preterminal illnesses (9).

In this regard, AF, an "old" arrhythmia that was first identified in 1909 (1), has assumed increasing scientific interest as the global demographic tide results in a burgeoning population of elderly individuals (10).

The European Society of Cardiology (ESC), the American Heart Association (AHA), and the American College of Cardiology (ACC) recognized the need to review the currently available information on AF, and produced guidelines for AF management (ACC/AHA/ESC guidelines on AF) (1, 11). Whilst these guidelines have been distributed from 2001, it remains unclear how well clinicians adhere to them (12, 13).

Negative impact of this growing epidemic on healthcare costs, quality of life, morbidity and mortality triggered the efforts to develop appropriate and cost-effective treatment strategies

(12). In this respect, introducing dronedarone as a novel and promising therapeutic entered into the market recently in the AF management.

The present study was designed to estimate the total cost of AF management with respect to clinical practice and available guidelines [American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines developed in conjunction with the European Society of Cardiology (ESC)] (1, 11) as well as to investigate if cost of therapy is offset by saving in the important cost drivers related to cardiovascular hospitalizations to provide data in relation to acute coronary syndrome (ACS), CHF, stroke and drug related adverse events encountered during AF treatment

## Methods

### Study design

This cost analysis study was based on the consensus opinion of the expert panel selected from physicians working as a cardiologist in Turkey on the total costs related to management of ACS, CHF, stroke and the drug related adverse events within the first month as well as within a year excluding the first month in patients with AF based on standardized questionnaire forms (shown in the Appendix A-D) filled by experts according to their daily clinical practice and also with respect to the recommendations available in the ACCF/AHA/ESC guidelines (1, 3, 13-21).

Cost items included in the questionnaire forms were treatment, healthcare resources utilization, and test and consultation items which provided a basis for the total cost calculation within the first month and within a year excluding the first month of AF diagnosis.

### First phase (filling of questionnaire forms according to daily clinical practice)

Of 1250 physicians working as a cardiologist in Turkey, a total of 20 experts, selected based on their clinical practice and scientific background, were acknowledged about the study via e-mail by the sponsor and then phoned to ask for a face-to-face interview. Seven experts from Adana, Ankara, İstanbul and İzmit who accepted the invitation were interviewed at their own institutions and filled the questionnaires in December 2009 -January 2010. The experts' median (min-max) age was 46.5 (42-58) years; they are all working at university hospitals from different cities of the country (Adana, Ankara, İstanbul and Kocaeli). Some experts filled all questionnaires while others answered some questions; however each questionnaire was filled at least by two experts.

### Second phase (expert panel)

Of 7 experts invited, 4 experts participated to the meeting during which questionnaires filled by 7 experts were re-viewed and cleared from contradictory misleading responses resulting from misunderstanding.

### Third phase (filling of questionnaire forms according to daily clinical practice)

Each of 4 experts attending to expert panel was asked to re-fill one of four questionnaire this time according to recommendations in the ACCF/AHA/ESC guidelines (1, 5, 13-21). Hence each questionnaire was filled by an expert according to guidelines.

Then, the total cost of management of co-morbid disorders and adverse events were calculated both with respect to expert's view and the guidelines.

### Questionnaire forms

The standardized questionnaire form was composed of cost items in the management of co-morbid disorders and drug related adverse events within the first month and within a year (excluding the first month) of AF treatment.

Items on co-morbid disorders included direct cost of management of ACS, CHF and stroke with respect to medical treatment, healthcare resources utilization (in-patient follow up for ICU, operation room and other services), test and consultation items per patient.

Items on drug related adverse events included direct cost of management of hypothyroidism, hyperthyroidism, neurological, dermatological, ophthalmological, gastrointestinal, hepatic, cardiac and pulmonary evidence and fatigue with respect to medical treatment, healthcare resources utilization (in-patient follow up) and test and consultation items per patient.

Since the questionnaire forms were filled according to expert's own view as well according to available guidelines, total cost of co-morbid disorders and drug related adverse events in AF management was calculated both for the daily clinical practice and the recommendations in the guidelines.

### Reference guidelines

Guidelines that provided a basis for the cost analysis included ACC/AHA/ESC 2006 Guidelines for the management of patients with AF (5), ESC 2010 Guidelines for the management of atrial fibrillation (1), 2011 ACCF/AHA/HRS focused update on the management of patients with AF (Updating the 2006 Guideline) (13), ACC/AHA key data elements and definitions for measuring the clinical management and outcomes of patients with AF (14), ACC/AHA 2007 Guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction (15), ACC/AHA 2008 performance measures for adults with ST-elevation and non-ST-elevation myocardial infarction (16), ACC/AHA Guidelines for the management of patients with ST-elevation myocardial infarction (17), ESC 2008 guidelines for the management of acute myocardial infarction in patients presenting with persistent ST-segment elevation (18), ESC 2008 Guidelines for the diagnosis and treatment of acute and chronic heart failure (19), ESC Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes (20) and ACC/AHA key data elements and definitions for measuring the clinical management and outcomes of patients with chronic heart failure (21).

### Cost analysis

Total medical costs were calculated including the associated cost items composed of treatment, healthcare resources utilization, and diagnostic test and consultation costs from SSI point of view. For drugs, retail prices from the updated price list and updated institution discount list of Social Security Institution (SSI) for 2010 were taken into account in calculation of the unit costs. Costs related to non-pharmacological treatments and tests were calculated considering the Health Implementation Notification by SSI. Hospitalization and consultation costs were calculated using unit prices also based on the same SSI notification.

Neither direct non-medical costs of different origin (e.g. transfers of patient and caregivers for examinations and/or hospitalization, home care, etc.) nor indirect costs (loss of productivity occurring as a result of a patient's inability to work) were included. The costs are provided in Turkish Lira (TL).

### Statistical analysis

Statistical analysis was made using computer software (SPSS version 13.0, SPSS Inc. Chicago, IL, USA). Medical expenses related to diagnosis, treatment, follow-up and management of AF related disorders and adverse events were the main parameter of the study. Cost model was based on the following equation: "Cost =  $\sum$  (Frequency; %) X (Unit price; TL)" (22). As central tendency measurement, both mean and median were calculated for all cost items. Although it is known that cost figures show non-normal distribution, mean cost was used for the whole group as it represents the disease burden better. Data were expressed as "mean, and median (min-max)".

## Results

### Co-morbid disorders

The average total cost of ACS was 5.478.43 TL (2.706.83 TL within the first month and 2.558.24 TL within a year excluding the first month) according to expert's view whereas it was 11.319.44 TL (3.534.78 TL within the first month and 7.784.67 TL within a year excluding the first month) when calculation was based on recommendations in the guidelines (Table 1).

The average total cost of CHF was 4.523.74 TL (2.435.75 TL within the first month and 2.087.99 TL within a year excluding the first month) according to expert's view whereas it was 2.925.86 TL (1.523.40 TL within the first month and 1.402.46 TL within a year excluding the first month) when calculation was based on recommendations in the guidelines (Table 1).

The average total cost of stroke was 5.719.25 TL (2.431.71 TL within the first month and 3.256.90 TL within a year excluding the first month) according to expert's view whereas it was 7.931.18 TL (4.933.91 TL within the first month and 2.997.28 TL within a year excluding the first month) when calculation was based on recommendations in the guidelines (Table 1).

### Drug related adverse events

Calculated based on expert's view vs. guidelines, total cost of management for hypothyroidism (62.80 vs. 118.06 TL), hyper-

**Table 1. Cost analysis of management of AF related disorders including acute coronary syndrome and congestive heart failure based on expert's view and recommendations in the guidelines**

| Variables                                 | Total cost (TL) / patient |                                  |                             |
|-------------------------------------------|---------------------------|----------------------------------|-----------------------------|
|                                           | Expert's view             |                                  | Guideline based             |
|                                           | Mean                      | Median (min-max)                 | Expert opinion <sup>1</sup> |
| <b>Acute coronary syndrome</b>            |                           |                                  |                             |
| Within the first month                    | 2.706.83                  | 2.404.21<br>(1.426.65-4.380.29)  | 3.534.78                    |
| Within a year (excluding the first month) | 2.558.24                  | 2.266.71<br>(1.313.79-4.150.52)  | 7.784.67                    |
| Total                                     | 5.478.43                  | 5.698.88<br>(2.816.78-8.530.81)  | 11.319.44                   |
| <b>Congestive heart failure</b>           |                           |                                  |                             |
| Within the first month                    | 2.435.75                  | 2.043.43<br>(1.858.97-3.517.89)  | 1.523.40                    |
| Within a year (excluding the first month) | 2.087.99                  | 2.267.61<br>(1.314.01- 2.557.41) | 1.402.46                    |
| Total                                     | 4.523.74                  | 4.465.53<br>(4.154.44-4.872.07)  | 2.925.86                    |
| <b>Stroke</b>                             |                           |                                  |                             |
| Within the first month                    | 2.431.71                  | 2.462.35<br>(1.718.37- 3.083.78) | 4.933.91                    |
| Within a year (excluding the first month) | 3.256.90                  | 3.256.90<br>(2.570.14- 3.943.66) | 2.997.28                    |
| Total                                     | 5.719.25                  | 5.719.25<br>(4.910.69-6.527.81)  | 7.931.18                    |

<sup>1</sup>These figures were calculated by a single expert for each indication reflecting the expensed if the treatment is done according to the recent guidelines

thyroidism (236.26 vs. 649.44 TL), neurological event (47.80 vs. 204.41 TL), dermatological event (10.12 vs. 11.68 TL), ophthalmological event (14.17 vs. 36.26 TL), gastrointestinal event (46.74 TL -only based on expert's view), hepatic event (50.76 vs. 169.57 TL), cardiac event (288.65 vs. 150.99 TL), pulmonary event (28.80 vs. 58.94 TL) and fatigue (27.55 vs. 34.39 TL) are given in Table 2.

## Discussion

There is considerable heterogeneity in 'real-life' management of AF (1,12-14). Accordingly, the marked difference in the costs calculated based on expert's view and guidelines concerning management in AF related disorders and adverse events in the present study is in line with the findings of a recent Euro Heart Survey (EHS) indicating a failure in the actual clinical management and therapy of AF to conform to the indications in ACC/AHA/ESC guidelines (1, 12-14).

According to our findings, total cost calculated for real life management of the ACS was almost half of the cost calculated based on guidelines. In fact, the deviation from guidelines is more predominant for the management of the disease within a year excluding the first month, since total cost calculated based

**Table 2. Cost analysis of management of adverse events related to drugs used in atrial fibrillation treatment based on expert's view and recommendations in the guidelines**

| Variables                          | Total cost (TL) / patient |                            |                             |
|------------------------------------|---------------------------|----------------------------|-----------------------------|
|                                    | Expert's view             |                            | Guideline based             |
|                                    | Mean                      | Median (min-max)           | Expert opinion <sup>1</sup> |
| <b>Drug related adverse events</b> |                           |                            |                             |
| Hypothyroidism                     | 62.80                     | 38.76<br>(38.76-155.43)    | 118.06                      |
| Hyperthyroidism                    | 236.26                    | 244.02<br>(202.74- 246.52) | 649.44                      |
| Neurological evidence              | 47.80                     | 47.80<br>(0.00-47.80)      | 204.41                      |
| Skin evidence                      | 10.12                     | 10.12<br>(0.00-10.12)      | 11.68                       |
| Eye evidence                       | 14.17                     | 10.12<br>(10.12-30.36)     | 36.26                       |
| Gastrointestinal evidence          | 46.74                     | 45.73<br>(45.73-50.79)     | -                           |
| Hepatic evidence                   | 50.76                     | 35.93<br>(35.93-80.41)     | 169.57                      |
| Cardiac evidence                   | 288.65                    | 424.91<br>(16.43- 429.92)  | 150.99                      |
| Pulmonary evidence                 | 28.80                     | 19.73<br>(14.52- 61.22)    | 58.94                       |
| Fatigue                            | 27.55                     | 15.18<br>(15.18- 52.28)    | 34.39                       |

<sup>1</sup>These figures were calculated by a single expert for each indication reflecting the expensed if the treatment is done according to the recent guidelines

on expert's view for this time period was one third of the guideline based cost. Therefore, while the real life management of ACS within the first month is compatible with the guidelines, long term management seem not to conform to the guidelines indicating a significant neglect in the clinical practice.

Besides, selection of early invasive treatment in ACS or in specific patient groups and related interventions and/or medications seems to be responsible for the great variation in the cost of treatment for ACS among the experts.

When expert's view and guideline recommendations were compared in terms of cost of HF, total cost of real life management of HF was determined to be almost two-fold of the cost based on guidelines. Based on increased cost indicating evidence of certain practices despite being unnecessary according to guidelines, clinicians seem not to adhere to guidelines in the real life management of HF both for the first month and in the rest of the year.

Considering stroke, total cost calculated for real life management of the disease was lower than the amount calculated with respect to recommendations in the guidelines. In fact, the deviation from guidelines is more predominant for the management of the disease during the first month, since total cost calculated based on expert's view was almost half of the guideline-based



cost in this time period. Therefore, while the real life management of stroke during entire year following the first month is compatible with the guidelines, short term management of the disease concerning the first month seems to be far from the guidelines despite the fact that most patients visiting cardiovascular specialist in ESC member countries were reported to have one or multiple associated medical conditions and specific stroke risk factors (1, 12-14).

For the most of drug related adverse events identified in the present study, lower costs were obtained for the calculations based on expert's view compared with guidelines. The only exception was the cardiac events since its management in the clinical practice was identified to be much more costly than indications in the guidelines.

Amongst various cardiac conditions associated with AF, CHF imposes the greatest risk of AF with a 4.5-fold increased risk in men and a 5.9-fold increased risk in women (23). Besides being diagnosed in 10% to 35% of patients with CHF during the course of the disease, AF was also reported to be associated with clinical severity of its symptoms (10).

Accordingly, possibly reflecting high awareness about the risk of this condition amongst physicians, as identified with higher costs based on expert's view, both CHF and cardiac adverse events seem to be managed in a manner exceeding the type and/or frequency of indications recommended in the guidelines. Nevertheless, the influence of socio-cultural background of patients on selection of appropriately individualized treatment or difference among physicians in the preference of USA or EU derived guidelines may also have a role in adherence to guidelines.

In Euro Heart Survey including 5,333 patients, it was indicated that risk factors for stroke were evident in 86% of patients while inconsistency between guidelines and clinical practice in stroke prevention and antiarrhythmic drug administration (12).

Two international, observational and cross sectional studies [RecordAF (REgistry on Cardiac rhythm disORDers) and REALISE-AF] among AF patients concerning patient profiles, co-morbid disorders and treatment strategies in the clinical practice of AF management revealed worldwide differences in patient profiles and practice patterns in AF management, general failure to control of disease leading high risk for hospitalization and cardiovascular events as well as significant differences in the clinical practice and guidelines with respect to antiarrhythmic and antithrombotic drug prescriptions (24, 25).

### Study limitations

Due to lack of readily reachable real life evidence/data for medical interventions in Turkey, expert panels are used as useful tools for estimation of treatment algorithms, costs of diseases. In this study, albeit low participation among the invited cardiologists in relation to certain factors such as work load or afraid of being criticized by the panel restricts to reach a conclusion to be generalized for the overall cost of AF in Turkey, use of expert opinions for estimation of AF management, related dis-

eases and the costs seems to be an alternative and acceptable way to estimate cost of this important health condition. No major limitation was faced during the study.

## Conclusions

In conclusion, reflecting the treatment algorithms in the management of AF as well as related adverse events in the clinical practice, our findings seem to emphasize the extra burden on health economics posed by patients suffering from the uncontrolled disease. Clarification of the epidemiology and natural history of the disease seems crucial to provide reasonable allocation of resources and the utilization of potentially exciting novel therapeutic alternatives that superimpose AF related adverse trends on mortality, morbidity and healthcare costs.

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## Appendix A. Acute Coronary Syndrome Questionnaire

We request your help about detecting of medical operations required to be performed for the following diseases within the bound of possibility, given the stated time intervals, based on these information, we will try to calculate a set of rough costs:

Numbers will completely represent expert opinion and experience. We may express the costs with numbers for operations and services and with fractional numbers for the performed operations and services. E.g. Two operation that considered to be used in one of two cases, may be expressed as 0,5.

During the recording of the services, the more detailed information is given, the more accurate data generate. Service lists of the Notice of Health Practice may be beneficial for the services.

### Acute Coronary Syndrome (ACS: First Month)

#### Potential services and their numbers within the first month (30 days) following diagnosis:

1. Average hospital stay apart from the intensive care?:
2. Average hospital stay during the intensive care?:
3. Imaging Operations (please specify the numbers one under the other along with the details). E.g. 10 contrast enhanced MRI or 2 three-dimensional MRI, 1/5 MR Angiography, etc.):
4. Surgery procedures (please specify the operation with the number and the possibility to be performed for patients (out of 100) one under another):
5. Special non-surgical operations [please specify the operation with the number and the possibility to be performed for patients (out of 100) one under another] (interventional radiological operations, angio operations, etc.)
6. Intensive Care procedures (monitorization, mechanic ventilation... etc. please record the number or the durations (day, hour) one under another):
7. Laboratory procedures (all routines along with the detailed special examinations as well as the potential numbers one under another):
8. Medication: Commercial title can be used, specify and record the utilization and the posologies within 30 days. *Record different and alternative protocols in separate lines.*
  - **Acute treatment protocols: (Name, posology, day):**
  - **Maintenance treatment protocols; (Name, posology):**
9. Examination, visit numbers performed by the physician (applicable only for the hospitalized patients, consider the control examinations of the patients discharged before the completion of 30 days period)
10. Other services, please record a definition and number for other operations and services with potential of practice within the first month.

### Acute Coronary Syndrome (ACS: One Year Average Excluding the First Month)

#### Except for the first month, numerical and clinic data for the average of first month in the stroke cases (consider the potential re-hospitalizations):

1. Average hospital stay apart from the intensive care?:  
*Give points to the potential re-hospitalizations out of 100 within the first year. What would the average day be for these admissions?*

2. Average hospital stay during the intensive care?:  
How many days would the patients re-hospitalized within one year spend their average admissions?
3. Imaging procedures (please specify the numbers one under the other along with the details). E.g. In case 2 control MRI are required within one year following the first month; express MRI as 2/12 months.
  - Potential imaging in re-hospitalizations (If the patient is re-hospitalized, list the potential imaging operations along with their number. Consider the average admission days):
  - **Routine follow-up imaging examinations:** (name of the operation along with the frequencies expressed as numbers performed in a day/month/year. If the frequency is low, it may be expressed as a fractional number as well, e.g. Express as 3/12 months for the operation performed 3 times in a year).
4. Surgery operations (for the patient re-hospitalized within one year/please specify the operation along with the number one after another):  
Specify the name of the operation and if it should be performed more than once, specify the number as well and the potential of re-practice during admission giving points to each out of 100. E.g. Cardiac tamponade drainage, 25/100 by thoracotomy
5. Special non-surgical operations (for the patients re-hospitalized within one year) (interventional radiological operations, angio operations, etc.)  
Specify the name of the operation and if it should be performed more than once, specify the number as well and the potential of re-practice during admission giving points to each out of 100.
6. Intensive Care Operations (for the patients re-hospitalized within one year) (monitorization, mechanic ventilation... etc. please specify the number or the durations (day, hour) one under another):
7. Laboratory operations (all routines along with the detailed special examinations as well as the potential numbers one under another)
  - Examinations required to be performed in re-hospitalizations (list the potential examinations with their numbers for the patient re-hospitalized within one year) Consider the average admission days):
  - **Routine follow-up examinations:** (name of the examination along with the frequencies expressed as numbers performed in a month. If the frequency is low, it may be expressed as a fractional number as well, e.g. Express as 3/12 months for the operation performed 3 times in a year).
8. Medication: Commercial title can be used, specify and record the utilization and the posologies within 30 days. Record different and alternative protocols in separate lines.
  - **Acute treatment protocols in potential re-hospitalizations: (Name, posology, day):**
  - **Maintenance treatment protocols; (Name, posology):** In case the data are the same as first-month-data, leave unrecorded.
9. Examinations performed by the physician (examinations expected to be performed for the control within one year).
10. Other services, please record a definition and number for other operations and services with potential of practice within the first year excluding the first month.

## Appendix B. Congestive Heart Failure Questionnaire

We request your help about detecting of medical operations required to be performed for the following diseases within the bound of



possibility, given the stated time intervals, based on these information, we will try to calculate a set of rough costs:

Numbers will completely represent expert opinion and experience. We may express the costs with numbers for operations and services and with fractional numbers for the performed operations and services. E.g. Two operation that considered to be used in one of two cases, may be expressed as 0,5.

During the recording of the services, the more detailed information is given, the more accurate data generate. Service lists of the Notice of Health Practice may be beneficial for the services.

### Congestive Heart Failure (CHF: First Month)

#### Potential services and their numbers within the first month (30 days) following diagnosis:

11. Average hospital stay apart from the intensive care?:
12. Average hospital stay during the intensive care?:
13. Imaging Operations (please specify the numbers one under the other along with the details). E.g. 10 contrast enhanced MRI or 2 three-dimensional MRI, etc.):
14. Surgery operations (please specify the operation with the number and the possibility to be performed for patients (out of 100) one under another):
15. Special non-surgical operations (please specify the operation with the number and the possibility to be performed for patients (out of 100) one under another) (interventional radiological operations, angio operations, etc.):
16. Intensive Care Operations (monitorization, mechanic ventilation... etc. please record the number or the durations (day, hour) one under another):
17. Laboratory operations (all routines along with the detailed special examinations as well as the potential numbers one under another):
18. Medication: Commercial title can be used, specify and record the utilization and the posologies within 30 days. Record different and alternative protocols in separate lines.
  - **Acute treatment protocols: (Name, posology, day):**
  - **Maintenance treatment protocols; (Name, posology):**
19. Examination, visit numbers performed by the physician (applicable only for the hospitalized patients, consider the control examinations of the patients discharged before the completion of 30 days period)
20. Other services, please record a definition and number for other operations and services with potential of practice within the first month.

### Congestive Heart Failure (CHF: One Year Average Excluding the First Month)

#### Except for the first month, numerical and clinic data for the average of first month in the stroke cases (consider the potential repeated hospitalizations):

11. Average hospital stay apart from the intensive care?:  
*Give points to the potential re-hospitalizations out of 100 within the first year. What would be the average day for these admissions?*
12. Average hospital stay during the intensive care?:  
How many days would the patients re-hospitalized within one year spend their average admissions?

13. Imaging procedures (please specify the numbers one under the other along with the details). E.g. In case 2 control MRI are required within one year following the first month; express MRI as 2/12 months.
  - Potential imaging in re-hospitalizations (If the patient is re-hospitalized, list the potential imaging operations along with their number. Consider the average admission days):
  - Routine follow-up imaging examinations: (name of the operation along with the frequencies expressed as numbers performed in a day/month/year. If the frequency is low, it may expressed as a fractional number as well, e.g. Express as 3/12 months for the operation performed 3 times in a year).
14. Surgery operations (for the patient re-hospitalized within one year/please specify the operation along with the number one after another):  
Specify the name of the operation and if it should be performed more than once, specify the number as well and the potential of re-practice during admission giving points to each out of 100. E.g. Cardiac tamponade drainage, 25/100 by thoracotomy
15. Special non-surgical operations (for the patients re-hospitalized within one year) (interventional radiological operations, angio operations, etc.)  
Specify the name of the operation and if it should be performed more than once, specify the number as well and the potential of re-practice during admission giving points to each out of 100.
16. Intensive procedures (for the patients re-hospitalized within one year) (monitorization, mechanic ventilation... etc. please specify the number or the durations (day, hour) one under another):
17. Laboratory procedures (all routines along with the detailed special examinations as well as the potential numbers one under another)
  - Examinations required to be performed in re-hospitalizations (list the potential examinations with their numbers for the patient re-hospitalized within one year) Consider the average admission days):
  - **Routine follow-up examinations:** (name of the examination along with the frequencies expressed as numbers performed in a month. If the frequency is low, it may expressed as a fractional number as well, e.g. Express as 3/12 months for the operation performed 3 times in a year).
18. Medication: Commercial title can be used, specify and record the utilization and the posologies within 30 days. *Record different and alternative protocols in separate lines.*
  - **Acute treatment protocols in potential re-hospitalizations: (Name, posology, day):**
  - **Maintenance treatment protocols; (Name, posology):** In case the data are the same as first-month-data, leave unrecorded.
19. Examinations performed by the physician (examinations expected to be performed for the control within one year).
20. Other services, please record a definition and number for other operations and services with potential of practice within the first year excluding the first month.

### Appendix C. Stroke Questionnaire

We request your help about detecting of medical operations required to be performed for the following diseases within the bound of possibility, given the stated time intervals, based on these information, we will try to calculate a set of rough costs:

Numbers will completely represent expert opinion and experience. We may express the costs with numbers for operations and services and with fractional numbers for the performed operations and services. E.g. Two operation that considered to be used in one of two cases, may be expressed as 0,5.

During the recording of the services, the more detailed information is given, the more accurate data generate. Service lists of the Notice of Health Practice may be beneficial for the services.

**Stroke;** (except for the traumatic ones, type of stroke is not significant, (hemorrhagic, occlusive...))

**Potential services and their numbers within the first month (30 days) following diagnosis:**

21. Average hospital stay apart from the intensive care?:
22. Average hospital stay during the intensive care?:
23. Imaging Operations (please specify the numbers one under the other along with the details). E.g. 10 contrast enhanced MRI or 2 three-dimensional MRI, etc.):
24. Surgery operations [please specify the operation with the number and the possibility to be performed for patients (out of 100) one under another]:
25. Special non-surgical operations [please specify the operation with the number and the possibility to be performed for patients (out of 100) one under another] (interventional radiological operations, angio operations, etc.)
26. Intensive Care Operations [monitorization, mechanic ventilation... etc. please record the number or the durations (day, hour) one under another]:
27. Laboratory operations (all routines along with the detailed special examinations as well as the potential numbers one under another):
28. Medication: Commercial title can be used, specify and record the utilization and the posologies within 30 days. Record different and alternative protocols in separate lines.
  - **Acute treatment protocols: (Name, posology, day):**
  - **Maintenance treatment protocols; (Name, posology):**
29. Examination, visit numbers performed by the physician (applicable only for the hospitalized patients, consider the control examinations of the patients discharged before the completion of 30 days period)
30. Other services, please record a definition and number for other operations and services with potential of practice within the first month.

**Stroke;** [except for the traumatic ones, type of stroke is not significant, (hemorrhagic, occlusive...)]

**Except for the first month, numerical and clinic data for the average of first month in the stroke cases (consider the potential repeated hospitalizations):**

21. Average hospital stay apart from the intensive care?:  
*Give points to the potential re-hospitalizations out of 100 within the first year. What would the average day be for these admissions (specify below the day spent in intensive care unit)?:*
22. Average hospital stay during the intensive care?:  
How many days would the patients re-hospitalized within one year spend their average admissions?
23. Imaging procedures (please specify the numbers one under the other along with the details). E.g. In case 2 control MRI are

required within one year following the first month; express MRI as 2/12 months.

- Potential imaging in re-hospitalizations (If the patient is re-hospitalized, list the potential imaging operations along with their number. Consider the average admission days):
  - Routine follow-up imaging examinations: (name of the operation along with the frequencies expressed as numbers performed in a day/month/year. If the frequency is low, it may be expressed as a fractional number as well, e.g. Express as 3/12 months for the operation performed 3 times in a year).
24. Surgery operations (for the patient re-hospitalized within one year/please specify the operation along with the number one after another):  
Specify the name of the operation and if it should be performed more than once, specify the number as well and the potential of re-practice during admission giving points to each out of 100. E.g. Intracranial hemorrhage drainage, 25/100 by craniotomy
  25. Special non-surgical operations (for the patients re-hospitalized within one year) (interventional radiological operations, angio operations, etc.)  
Specify the name of the operation and if it should be performed more than once, specify the number as well and the potential of re-practice during admission giving points to each out of 100.
  26. Intensive Care Operations (for the patients re-hospitalized within one year) [monitorization, mechanic ventilation, etc. please specify the number or the durations (day, hour) one under another]:
  27. Laboratory operations (all routines along with the detailed special examinations as well as the potential numbers one under another)
    - Examinations required to be performed in re-hospitalizations (list the potential examinations with their numbers for the patient re-hospitalized within one year) Consider the average admission days):
    - **Routine follow-up examinations:** (name of the examination along with the frequencies expressed as numbers performed in a month. If the frequency is low, it may expressed as a fractional number as well, e.g. Express as 3/12 months for the operation performed 3 times in a year).
  28. Medication: Commercial title can be used, specify and record the utilization and the posologies within 30 days. Record different and alternative protocols in separate lines.
    - **Acute treatment protocols in potential re-hospitalizations: (Name, posology, day):**
    - **Maintenance treatment protocols; (Name, posology):** In case the data are the same as first-month-data, leave unrecorded.
  29. Examinations performed by the physician (examinations expected to be performed for the control within one year).
  30. Other services, please record a definition and number for other operations and services with potential of practice within the first year excluding the first month.
  31. Name of the potential physiotherapy operations and the information about how many and how long the operations can be administered.

**Appendix D. Undesirable Adverse Effects Questionnaire**

*An elaboration will be performed for the operations and services during the presentation provided for undesirable adverse effects when*

the cardiovascular drugs including Dronedarone, Amiodarone, Sotalol and Flecainide are used. Specially focused undesirable adverse effects are respectively as follows:

1. Hypothyroidism
2. Hyperthyroidism
3. The cases developing neurological symptoms (tremor, sleeping disorders)
4. The cases developing skin problems (photosensitivity)
5. The cases developing eye problems (photophobia, visual disorder(blurred vision))
6. The cases developing gastrointestinal problems (Diarrhea, nausea, vomiting)
7. The cases developing hepatic problems
8. The cases developing cardiac problems (bradycardia, tachycardia, proarrhythmia)
9. The cases developing pulmonary problems (dyspnea)
10. Fatigue

Consider mainly the operations to be performed during acute period. Add your opinion to "General approaches and notes" under the title of the corresponding side effects for the case types which, in your opinion, requires follow-up without operation or service.

#### 1. Hypothyroidism:

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express separately):

#### Diagnostic operations: (all image and laboratory operations)

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

#### Treatment operations: (if available)

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

#### Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

#### General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).

#### 2. Hyperthyroidism

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express separately):

#### Diagnostic operations: (all image and laboratory operations)

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

#### Treatment operations: (if available)

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

#### Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

#### General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).

#### 3. The cases developing neurological symptoms (tremor, sleeping disorders)

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express separately):

#### Diagnostic operations: (all image and laboratory operations)

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

#### Treatment operations: (if available)

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

#### Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

#### General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).

#### 4. The cases developing skin problems (photosensitivity)

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express separately):

#### Diagnostic operations: (all image and laboratory operations)

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Treatment operations: (if available)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Pharmaceutical treatment protocols (fill out if necessary; give points to the possibility out of 100 if relatively necessary):**

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

**General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).**

**5. The cases developing eye problems (photophobia, visual disorder (blurred vision))**

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express as days separately):

**Diagnostic operations: (all image and laboratory operations)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Treatment operations: (if available)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):**

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

**General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).**

**6. The cases developing gastrointestinal problems (Diarrhea, nausea, vomiting)**

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express as days separately):

**Diagnostic operations: (all image and laboratory operations)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Treatment operations: (if available)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):**

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

**General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).**

**7. The cases developing hepatic problems**

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express as days separately):

**Diagnostic operations: (all image and laboratory operations)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Treatment operations: (if available)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):**

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

**General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).**

**8. The cases developing cardiac problems (bradycardia, tachycardia, proarrhythmia)**

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express as days separately):

**Diagnostic operations: (all image and laboratory operations)**

For the outpatients to be followed-up (operation, number and time interval):



For the inpatients to be followed-up (operation, number and time interval):

**Treatment operations: (if available)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):**

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

**General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).**

**9. The cases developing pulmonary problems (dyspnea)**

**Possibility of hospitalization** (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express as days separately):

**Diagnostic operations: (all image and laboratory operations)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Treatment operations: (if available)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):**

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

**General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).**

**10. Fatigue**

Possibility of hospitalization (assign a possibility out of 100), number of days for the possible hospital stay (intensive care/if normal separate bed system is available, express as days separately):

**Diagnostic operations: (all image and laboratory operations)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Treatment operations: (if available)**

For the outpatients to be followed-up (operation, number and time interval):

For the inpatients to be followed-up (operation, number and time interval):

**Pharmaceutical treatment protocols (fill out if necessary, give points to the possibility out of 100 if relatively necessary):**

For the outpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

For the inpatients to be followed-up (use separate lines for different protocols) (express as the name and the posology of the drug):

**General approaches and notes: (if available, express the follow-up protocols for such patients and, if not available, express your general approach).**