CHAPTER 4

EMPIRICAL RESULTS

4.1 The Data

The two hundred medical records and corresponding prescriptions eligible for the study were reviewed in order to check the existence of treatment variations between actual practice and recommendations of the guideline.

The data collected facilitated to draw some information on the general drug prescribing pattern mainly antibiotic prescribing compliance with the guideline. Associated cost of prescriptions that did not comply with recommended treatment in the guideline was estimated. Raw data was put into a spreadsheet and summarized. Results of the study are presented below. It should be noted through out this document that the term compliance is used to describe prescribing practices conforming or matching with recommendations of the guideline.

Number of patients by sex and age group in the study sample (n=200) is shown on Table 4.1.Out of the total number of patients, the review indicated that 55 % of the children were male and 45 % female. Age of children in the study sample was divided into three groups i.e. below 5, between 5 and 10, and above 10 and below 15 years of age. The numbers of children below 5 years of age accounted 78.5 % (157 out of 200 cases). Obviously this indicates that children below 5 years of age are more vulnerable to AURI than the other groups.

Table 4.1: Number of Patients by Sex and Age Groups

Age group	Sex		Total
	Male	Female	
0 - up to 5	86 (54.8) [43.0]	71 (45.2) [35.5]	157 (100.0) [78.5]
Greater than 5 - 10	18 (58.1) [9.0]	13 (41.9) [6.5]	31 (100.0) [15.5]
Greater than 10 - below 15	6 (50.0) [3.0]	6 (50.0) [3.0]	12 (100.0) [6.0]
Total	**110** **(55.0)** **[55.0]**	**90** **(45.0)** **[45.0]**	**200** **(100.0)** **[100.0]**

Notes: ( ) = percentage share of each age group

[ ] = Percentage share of the total number

Review of medical records using the pre-defined criteria indicated that 14 % of the total cases were categorized as bacterial AURI, which implies that majority of the cases (86 %) were due to non-bacterial (viral) etiology (Table 4.2). The findings from this study with respect to etiology of AURI confirm with review of literature that most AURI cases are viral in origin. The accuracy of diagnosis whether it is a bacterial or viral AURI is the foundation of subsequent decisions of the physician to prescribe or not to prescribe an antibiotic. As often is the case, apart from the confusion between bacterial and viral signs and symptoms presented by the patient, the decision to prescribe is subjected to several factors including clinical experience, severity of illness, history of prior antibiotic medication, drug resistance pattern and diagnostic and laboratory susceptibility tests. The availability of diagnostic and laboratory susceptibility testing facilities could help, but are expensive and could not be used widely. However, from economic and public health point of view, the use of basic diagnostic facilities to enhance identification of bacterial AURI cases where

there seem to be no clear cut demarcation warrant a research with respect to the growing concern of antimicobial resistance. Provision of these facilities maybe more cost effective method (Peter et al., 1992) for dealing with the problem than introducing newer, more expensive drugs with relatively limited information about safety and efficacy.

Table 4.2: Number of Patients by Age Group and Diagnosis

Age group	Diagnosis		Total
	Bacterial	Non bacterial	
0 - up to 5	21 (13.4)	136 (88.6)	157 (100.0)
Greater than 5 - 10	5 (16.1)	26 (83.9)	31 (100.0)
Greater than 10 - below 15	2 (16.7)	10 (83.3)	12 (100.0)
Total	**28 (14.0)**	**172 (86.0)**	**200 (100.0)**

Note: ( ) = percentage share of each age group

Review of data indicated that 9 % (18 out of 200 cases) received prior antibiotic medication (Table 4.3). Prior antibiotic treatment in the context of Thailand could be associated with self-medication. Physicians' knowledge about prior antibiotic medication that may affect the clinical signs has influence on the decision of the physician on prescribing and choosing the type of antibiotic. As stated else where in this study, antimicrobial drug resistance has become a major threat to public health. Therefore, physicians have a greater role in educating the patient and parents to refrain from unnecessary self-medication with antibiotics. Among all age groups, children below 5 years were reported to have higher rate of prior history of antibiotic medication (14 out of 18 cases).

Table 4.3: Number of Patients by Age Group Who Had History of Prior Antibiotic Medication (within 3 days)

Age group	Prior antibiotic history		Total
	Yes	No	
0 - up to 5	14 (8.9) [7.0]	143 (91.1) [71.5]	157 (100.0) [78.5]
Greater than 5 – 10	2 (6.5) [1.0]	29 (93.5) [14.5]	31 (100.0) [15.5]
Greater than 10 – below 15	2 (16.7) [1.0]	10 (83.3) [5.0]	12 (100.0) [6.0]
Total	**18** **(9.0)** **[9.0]**	**182** **(91.0)** **[91.0]**	**200** **(100.0)** **[100.0]**

Notes: ( ) = percentage share of each age group

[ ] = percentage share of the total number

As shown in Table 4.2, 14 % of the total cases were categorized under bacterial AURI, whereas out of the total cases reviewed 46 % had received antibiotics (Table 4.4). This is an important point to consider in view of minimizing unwanted adverse drug events, containing antimicrobial drug resistance and minimizing increasing cost of prescriptions that might be arising from indiscriminate use of antibiotics for mild AURI in children. A recent study made by WHO reported that for every 100 respiratory infections, 20 % require antibiotic treatment (WHO, 2000). The overall finding in this study is relatively higher with respect to the global estimation. The higher percentage of antibiotic prescribing can partly be associated with the different levels of experience and categories of doctors practicing at the general pediatric OPD in King Chulalongkorn Memorial Hospital. The average number of drugs prescribed per patient was 2.65 items and the average cost per prescription was 70 baht.

Table 4.4: Number of Patients by Age Group and Prescriptions Containing Antibiotic

Age group	Prescriptions containing antibiotic		Total
	Yes	No	
0 – up to 5	71 (45.2)	86 (54.8)	157 (100.0)
Greater than 5 – 10	13 (41.9)	18 (58.1)	31 (100.0)
Greater than 10 – below 15	8 (66.7)	4 (33.3)	12 (100.0)
Total	**92 (46.0)**	**108 (54.0)**	**200 (100.0)**

Note: ( ) = percentage share of each age group

Table 4.5 indicates that staff doctors who are mainly from the medical faculty and some from Thai Red Cross Society treated 57.5 % (115 out of 200 cases) of patients, fellows 5 %, residents 33.5 %, and externs the remaining 4 %. From this, it can be said that almost one out of two patients treated by a staff or fellow doctor receives an antibiotic.

For clear understanding of the different categories of doctors practicing in the hospital, it will be important to describe each category as follows:

- Staff doctors are those who are employed by the University but working for the Thai Red Cross Society and train medical doctors, this group also includes doctors who are employed by Thai Red Cross Society.

- Fellow doctors are qualified pediatricians being trained to be sub-specialists in any particular field of pediatrics.

- Residents are doctors who are under training for specialization in general pediatrics in order to be qualified pediatricians.

- Externs are 6th year medical students.

With this background information, the distribution of prescriptions containing antibiotics with respect to physician status was reviewed and presented in Table 4.5.

Table 4.5: Number of Antibiotic Containing Prescriptions According to Physician Status

Physician status	**Prescriptions containing antibiotic**		**Total**
	Yes	**No**	
Staff	53 (46.1)	62 (53.9)	115 (100.0) [57.5]
Fellow	5 (50.0)	5 (50.0)	10 (100.0) [5]
Resident	28 (41.8)	39 (58.2)	67 (100.0) [33.3]
Extern	6 (75.0)	2 (25.0)	8 (100.0) [4]
Total	**92** **(46.0)**	**108** **(54.0)**	**200** **(100.0)** **[100]**

Notes: ( ) = percentage share of physician status

[ ] = percentage share of total number of prescriptions by physician status

Tables 4.4 and 4.5 provide more or less similar information, but observations are presented from different perspective. Compliance of antibiotic prescribing with the recommendations of the guideline was reviewed using the predefined criteria described in Chapter 3. Overall, 37.5 % (Table 4.6) of the total prescriptions did not comply with the recommendations of the guideline. The non-compliance observed was mainly due to prescribing of antibiotics for non-bacterial AURI and it was more apparent among staff and fellow doctors than in residents and externs. King Chulalongkorn Memorial Hospital being one of the biggest teaching hospitals in Thailand; staff doctors should therefore strive to demonstrate best practices for the medical students who take them as a role model.

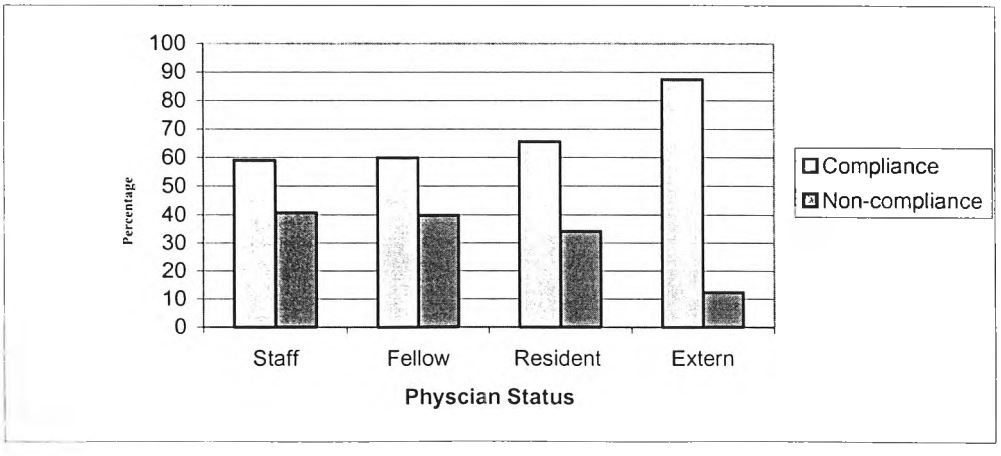
The finding in this study could help the hospital management to direct its efforts in designing and introducing intervention mechanisms to improve prescribing compliance to the guideline with more emphasis for specific category of physicians.

Table 4.6: Number of Prescriptions by Physician's Status and Antibiotic Prescribing Compliance

Physician status	Compliance to the guideline		Total
	Yes	No	
Staff	68 (59.1)	47 (40.9)	115 (100.0)
Fellow	6 (60.0)	4 (40.0)	10 (100.0)
Resident	44 (65.7)	23 (34.3)	67 (100.0)
Extern	7 (87.5)	1 (12.5)	8 (100.0)
Total	**125 (62.5)**	**75 (37.5)**	**200 (100.0)**

Note: ( ) = percentage share of physician status

Figure 4.1: Percentage of Compliance and Non-compliance with Guideline by Physician Status



Source: Table 4.6

Table 4.7 summarizes the antibiotic prescribing compliance in children of all age group. Among children below 5 years of age, majority (64.3 %) received antibiotic treatment complying to the guideline, however, 35.7 % of the prescriptions for children below 5 years of age did not comply with recommendations of the guideline. Given that children below 5 years of age constitute the largest group, emphasis should be given to select and implement appropriate interventions to improve compliance with the guideline for this group.

Table 4.7: Number of Patients by Age Group and Percentage of Compliance with the Guideline

Age group	**Compliance to the guideline**		**Total**
	Yes	**No**	
0 - up to 5	101 (64.3)	56 (35.7)	157 (100.0)
Greater than 5 - 10	18 (58.1)	13 (41.9)	31 (100.0)
Greater than 10 – below 15	6 (50.0)	6 (50.0)	12 (100.0)
Total	**125 (62.5)**	**75 (37.5)**	**200 (100.0)**

Note: ( ) = percentage share of each age group

Overall 46 % (92 out of 200 cases) of patients received antibiotic. Of the total patients diagnosed with bacterial AURI, 85.7 % (24 out of 28 cases) were compliant to the guideline whereas 39.5 % (68 out of 172 cases) classified as non-bacterial AURI, were not compliant to the guideline recommendation (Table 4.8).

Table 4.8: Percentages of Prescriptions Containing Antibiotic by Type of Diagnosis

Diagnosis	Prescriptions containing antibiotic		Total
	Yes	No	
Bacterial	24 (85.7)	4 (14.3)	28 (100.0)
Non bacterial	68 (39.5)	104 (60.5)	172 (100.0)
Total	**92 (46.0)**	**108 (54.0)**	**200 (100.0)**

Note: ( ) = percentage share of diagnosis

The two types of non-compliance to the guideline noted above are explained in the following section.

4.1.1 Type I non-compliance: Patients who should have gotten antibiotic treatment but not prescribed

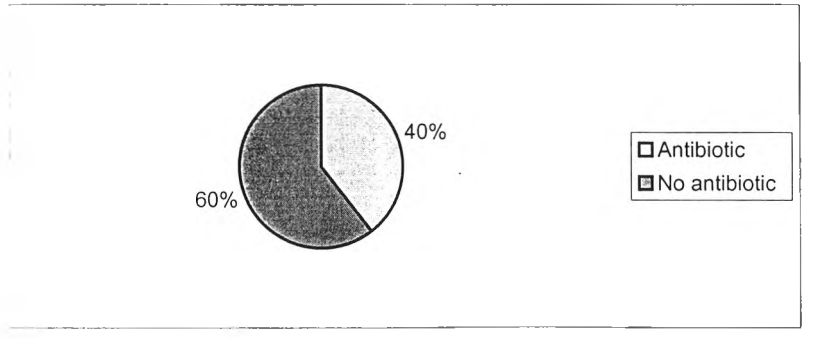
According to the guideline, twenty-eight patients in this category had suggestive history and clinical findings compatible with the criteria for diagnosis of bacterial AURI, this group of cases need to be treated with antibiotic. But, 14.3 % (4 out of 28 cases) of the patients being classified as bacterial AURI did not receive antibiotic treatment (Table 4.8). This means that the disease was not cured and patients might continue to suffer from the sickness. As a result, in the short term, the charge that the patient paid is underestimated than what it should be. As the illness continues, the patient may want to visit a doctor again, which could increase the cost of treating the disease.

4.1.2 Type II non-compliance: Patients who should not have been entitled to receive antibiotic but prescribed

Patients in this category were those with non-bacterial AURI, but received antibiotic when the guideline does not recommend. 39.5 % (Table 4.8) of patients (68 out of 172 cases) who had history and clinical signs compatible with non-bacterial AURI received antibiotic treatment. The immediate charge that the patient paid for the prescribed antibiotic will be higher than what the patient should have paid. In the long-term, the cost of treating non-bacterial AURI with an antibiotic when not therapeutically justified contributes to the emergence of antimicrobial resistance that will have serious health and economic implications. The occurrence of unwanted adverse drug events, due to unnecessary antibiotic treatment could be minimized if patients receive appropriate treatment.

In both the above cases, non-compliance to the guideline was noted. From patient, health care provider and societal perspectives, short and long-term cost implications of non-compliance type II are discussed in Sections 4.3.1 and 4.3.2 respectively.

Figure 4.2: Percentage of Antibiotic Containing Prescriptions for Non-bacterial AURI



Source: Table 4.8

4.2 Analysis

As stated in Chapter 3, cases were classified as bacterial and non-bacterial AURI using the predefined criteria and prices of prescriptions were collected from a computer database in the hospital pharmacy. Prescriptions were then categorized into two groups, complying with the guideline and those not complying with the guideline. The analysis was based on the total price of prescriptions containing antibiotics in the two groups. The Mann Whitney rank sum test (Glantz, 1992) was used to test the difference between the two group means.

4.2.1 Difference between actual practice and guideline recommendations

The mean total prices of prescriptions was computed and analyzed using the Mann Whitney rank sum test to compare the means from the compliance and non-compliance groups. Age is one factor considered for calculation of doses and amount of drug to be prescribed for a particular patient, thus age of a child could affect the price of prescriptions, generally, larger amount of drug is required for children above 5 years of age than children below 5 years of age. Age could therefore be considered as one possible confounding factor while calculating the mean total price, to rule out this effect, comparison was done among children below 5 years of age. Considering the above condition, the two mean total prices of compliance and non-compliance group to the guideline among children below 5 years of age were found to be 16 baht and 47.23 respectively. As a result a difference of 31.23 baht (47.23 minus 16) per case was noted.

In a similar manner, calculation was made for children above 5 years of age. The mean total price of prescription for non-bacterial AURI (non-compliance group) was 74.11 baht and for the compliance group it was 25.63 baht, and a difference of 48.48 baht per case was found (higher than children

above 5 years). The pattern is similar in children below and above 5 years of age. From this, it can be said that the difference was not because of age, but the mean total price difference was due to variations in prescribing practices.

Mann Whitney rank sum test indicates that in both age groups there is a statistically significant difference between the compliance and noncompliance group means (p-value < 0.01). The difference noted above is used to estimate the cost saving that can be made if treatment provided to children with non-bacterial AURI could be compliant to the guideline recommendation.

4.2.2 Estimating cost savings

It was found that the mean total price paid by the two groups of patients of age below 5 years, i.e. one group receiving antibiotic prescriptions complying to the guideline and the other group receiving prescriptions not complying to the guideline was 16 and 47.23 baht respectively.

After the Mann Whitney rank sum test, it was noted that there is statistically significant difference (Mann-Whitney U, $p<0.05$) between the two groups. This can explain that a patient receiving prescription not compliant to guideline could save 31.23 baht per case if he/she received drugs as per the guideline recommendation. For the group of 0-5 years, 56 cases were not compliant. Therefore savings from this group was estimated to be 31.23 baht x 56 cases = 1,748.88 baht. Similarly, for the group with age above 5 years, savings was estimated as 48.48 baht x 19 cases = 921.22 baht. For the whole study group, saving was 31.23 baht x 75 cases = 2,342.55 baht which is approximately equivalent to 53 US dollar (an exchange rate of 44 baht per US$).

4.3 Discussion

The active surveillance data (1990 to 1995) obtained from the MOPH, ARIC, TB division, revealed that 35.6 to 63 % of the Upper Respiratory Infection (URI) cases are generally treated with antibiotics, the maximum being at community hospitals and the minimum at regional hospitals (MOPH, 1999).

Findings from this study indicates that 86 % (Table 4.2) of children were found to have non-bacterial (viral) AURI and 37.5 % (Table 4.6) of the total prescriptions were not compliant to guideline recommendations. The results in this study are consistent with the study cited here above. However, as analysis was based upon a relatively small and non-randomly selected sample of prescriptions and medical records statistical results should be interpreted with caution.

Analysis of the two group means of total price of prescriptions containing antibiotics (compliance and non-compliance groups) indicates that non-compliance is more costly than compliance to guideline recommendations. The mean total prices of the two groups were computed compared and the difference was statistically significant. This difference can be attributed to variations in prescribing practice of doctors. Age was considered as a possible confounding factor, despite differences in age group, the charge paid for prescriptions for non-compliance group was higher than the compliance group in children below and above five years of age. The variation in prescribing (non-compliance) has implication on health and cost of treatment, in particular, the use of antibiotics in viral infections is not recommended in the guideline and has no therapeutic benefit, instead it may have cost implications on health and exhaust limited resources that could be used for essential health care. Given its economic and public health significance, short and long-term cost implications of type II non-compliance described above are discussed here.

Two important aspects of antimicrobial drug use, which ultimately cost institutions large amount of money, are antibacterial-induced complications and development of antibacterial resistant strains of microorganisms. Prevention of these two consequences has an important influence on patient survival and costs (Hasset et al., 1997). The use of antibiotics indiscriminately apart from contributing to the development of resistance causes adverse drug events. Adverse Drug Events (ADE) occur frequently and lead to a significant number of fatalities each year. It has been estimated (Arakelian et al., 1999) that fatalities directly attributable to adverse drugs reactions are the fourth to sixth leading causes of death in US hospitals, exceeding causes by pneumonia and diabetes. The economic burden resulting from drug related morbidity and mortality is equally significant and has been conservatively estimated at US 30 billion dollars annually and could exceed US 130 billion in a worst-case scenario. Prevention of drug-related morbidity and mortality has therefore become an increasingly important requirement for reducing healthcare expenditure. Antibacterial are commonly identified among the leading causes of ADE. The cost of drug-related adverse events are significant, depending on the perspective, the costs may vary substantially, although most studies present the economic impact from the perspective of the institution. ADE result in hospitalizations, increased length of hospital stay and an increase in an overall healthcare utilization costs. Generally, the cost implication of non-compliance in this case can be viewed in two ways, its short and long-term cost implications.

4.3.1 Short-term cost implications

In the short-term, the cost of prescriptions containing antibiotics for viral AURI (non-compliance) will be high while antibiotics are not recommended and do not worth prescribing. This in turn affect patients who pay prescription bills out of pocket or paid through social welfare organizations or insurance schemes

or health care providers. Therefore, minimizing health care expenditure through improving the quality of health care is a major concern to all. The trends of health services in Thailand are rising to cover all the people under such schemes as the revolving fund for medical services, voluntary health insurance, social security, student's health insurance, workmen's compensation fund, and insurance for road traffic accident victims. As of 1998, approximately 80.3 % of Thai people have been covered with health insurance of one scheme or another (MOPH, 2000). Currently King Chulalongkorn Memorial Hospital recover the cost of drugs from prescription charges, but in the years to come like many other hospitals in Bangkok, it is moving towards providing medical coverage through one or more of these insurance schemes, therefore containing escalating cost of prescriptions maybe a priority area to deal with. Implementation of clinical guidelines with other interventions could then be one of the means to facilitate the attempt to improve the quality of care and minimize health care expenditure.

No study has been done in King Chulalongkorn Memorial Hospital to document and cost drug related adverse events especially due to unnecessary use of antibiotics in children with AURI; this could be one of the areas that require further research.

4.3.2 Long-term cost implications

The issue of drug resistance among bacteria adds a unique dimension to the pharmacoeconomics of antibacterial treatment. The prevalence of bacterial resistance among bacteria is positively linked to the overall use of antibacterial drugs in one patient must include the possible failure of treatment of other patients because of the spread of drug resistance among bacteria. This is in addition to the opportunity cost of the resources consumed by the treatment itself (Peter et al., 1992).

A study made at Siriraj hospital in 1987, one of the teaching hospitals in Thailand, indicated that 83 % of children with acute respiratory tract infection were given an oral antibiotic. According to verbal surveillance of the study group, the antimicrobial prescriptions for non-streptococcal URI at various hospitals and medical centers in Thailand was considerably high and varied within the range of 70 to 98 % (Artavetakun et al., 1996 citing Nirun Vanprapa, 1987). The results from this study similarly indicated the existence of non-compliance to guidelines and prescribing of antibiotic for treating children with AURI, and suggest that the degree of compliance of antibiotic treatment to clinical guidelines needs an improvement.

Increasing antimicrobial resistance has presented a scientific challenge and economic opportunity to the pharmaceutical industry for the development of new antimicrobial agents. New antibiotics are continually being sought through research and development, and compounds that can provide alternative treatment for a number of infections are made available by the pharmaceutical industry especially for those caused by antibiotic resistant strains of bacteria. Development of new drug is one solution to the problem of resistance, but it may be an expensive one. Apart from the cost of development of new drugs, there is the distinct possibility that they may not be as effective as the drugs that we already have (Peter et al., 1992). However, if a reasonable rate of return cannot be foreseen, capital for research and development is likely to be invested in areas that appear more financially attractive (Peter et al., 1992 citing Liss and Batchelor, 1987).

In the era of trade globalization, antibiotic resistant strains of bacteria can easily spread from one country to the other, and the scale of the problem becomes more complicated. The long-term cost implication of drug resistance could be devastating, supposing that currently existing antibiotics become ineffective due to resistant strains of bacteria resulting from indiscriminate use

of antibiotics, hence, it will be very hard to imagine medical practice without antibiotics.

The debate about potential harmful effects of unnecessary treatment with antibacterial drugs has tended to focus on rare, serious side effects, whereas, literature suggests that inappropriate use of antibacterial drugs to treat viral infections actually encourages secondary bacterial infections by harming the normal flora of the body and allowing pathogenic bacteria to take advantage of the general immuno-suppression which follows viral infection. All aspects of management should be subjected to economic analysis to ask who is benefiting from this use of resources and by how much (Peter et al., 1992).

The problem of non-compliance with guideline and consequent prescribing of antibiotic unnecessarily should therefore be addressed critically in order to contain the wide spreading antimicrobial resistance, cost of drug related adverse events and escalating cost of treatment in general. The issue of emergence of antibacterial resistant strains of microorganisms is critical and concerted effort of the hospital management staff, physicians and policy makers to address the cost implications on health and the economy.

One among other tools to improve appropriate use of antibiotics is through effective implementation of guidelines. Effective implementation of guidelines requires participation of all stakeholders including management staff, doctors, pharmacists, nurses and other personnel involved in the health care delivery. A thorough understanding of all the constraints and enabling factors will facilitate the effort to improve compliance to guidelines. The national guideline for the management of AURI was developed with the intention to improve quality of care and standardized treatment provided to children with AURI; however, its effective implementation requires intensive follow up and further study. The findings from this study demonstrated that compliance to the guideline could be used to save limited resources.

Given the limitations of this study mentioned elsewhere, the findings highlighted the short and long-term cost implications of non-compliance, and its seriousness, however, further research is required to come up with concrete figures or estimates of the cost implication of antimicrobial resistance in particular.

In conclusion, this study indicates that majorities of children with AURI were below 5 years of age and most cases were non-bacterial origin. A total of 2,342.25 baht could be saved for non-compliance group of cases in the study sample, if treatment variations (non-compliance) can be avoided and children with non-bacterial AURI treated according to the guideline. The overall antibiotic prescribing pattern was 46 %, and this requires a special attention. Staff doctors constituted the largest group in which antibiotic prescribing practice did not comply with the recommendations of the guideline. The highest percentage of prior antibiotic medication was observed among children below 5 years of age. This could be one possible reason why the staff doctors prescribed antibiotic to cases compatible with viral etiology while it was not recommended in the guideline. In this connection, educating parents could help to minimize the use of antibiotics in treating children with AURI before examination by a doctor. Wide dissemination and promotion of the national guideline, monitoring its utilization, provision of continuing medical education and objective drug information on drugs and antibiotic resistance patterns to doctors, pharmacists, nurses, review of prescriptions and medical records and feedback to prescribers should be emphasized. Physicians, pharmacists and all other health workers involved in the drug use process need to join their hands and work together to effectively implement clinical guidelines, develop suitable cost-effective intervention(s) that could help limit the unnecessary use of antibiotics for viral AURI in King Chulalongkorn Memorial Hospital.