Research Article

Application of DMAIC Cycle and Modeling as Tools for Health Technology Assessment in a University Hospital

Alfonso Maria Ponsiglione 1, Carlo Ricciardi 2, Arianna Scala 3, Antonella Fiorillo 2, Alfonso Sorrentino 4, Maria Triassi 3, Giovanni Dell’Aversana Orabona 4, and Giovanni Improta 3

1Department of Electrical Engineering and Information Technology (DIETI), University of Naples "Federico II", Naples, Italy
2Department of Advanced Biomedical Sciences, University of Naples "Federico II", Naples, Italy
3Department of Public Health, University Hospital of Naples "Federico II", Naples, Italy
4Maxillofacial Surgery Unit, Department of Neurosciences, Reproductive and Odontostomatological Sciences, University Hospital of Naples "Federico II", Naples, Italy

Correspondence should be addressed to Arianna Scala; ariannascala7@gmail.com

Received 15 July 2020; Accepted 10 August 2021; Published 18 August 2021

Academic Editor: Daniel Espino

Copyright © 2021 Alfonso Maria Ponsiglione et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. The Health Technology Assessment (HTA) is used to evaluate health services, manage healthcare processes more efficiently, and compare medical technologies. The aim of this paper is to carry out an HTA study that compares two pharmacological therapies and provides the clinicians with two models to predict the length of hospital stay (LOS) of patients undergoing oral cavity cancer surgery on the bone tissue. Methods. The six Sigma method was used as a tool of HTA; it is a technique of quality management and process improvement that combines the use of statistics with a five-step procedure: "Define, Measure, Analyze, Improve, Control" referred to in the acronym DMAIC. Subsequently, multiple linear regression was used to create two models. Two groups of patients were analyzed: 45 were treated with ceftriaxone while 48 were treated with the combination of cefazolin and clindamycin. Results. A reduction of the overall mean LOS of patients undergoing oral cavity cancer surgery on bone was observed of 40.9% in the group treated with ceftriaxone. Its reduction was observed in all the variables of the ceftriaxone group. The best results are obtained in younger patients (−54.1%) and in patients with low oral hygiene (−52.4%) treated. The regression results showed that the best LOS predictors for cefazolin/clindamycin are ASA score and flap while for ceftriaxone, in addition to these two, oral hygiene and lymphadenectomy are the best predictors. In addition, the adjusted $R^2$ showed that the variables considered explain most of the variance of LOS. Conclusion. SS methodology, used as an HTA tool, allowed us to understand the performance of the antibiotics and provided variables that mostly influence postoperative LOS. The obtained models can improve the outcome of patients, reducing the postoperative LOS and the relative costs, consequently increasing patient safety, and improving the quality of care provided.

1. Introduction

Healthcare seeks to give improvements in the prevention, control, and treatment of diseases, but at the same time, it also deals with complications, inefficiencies, and other problems that put patients' safety at risk. Therefore, it is necessary to monitor the health services provided by applying management methods and tools to control quality [1]. Nowadays, several methodologies and approaches are used in healthcare to help in the clinical decision-making process [2–8], to aid physicians in defining the diagnosis and prognosis of patients [9–11], and to analyze quality improvement in hospital processes [12, 13]. A useful methodology for these purposes is the Health Technology Assessment (HTA), a multidisciplinary process for medical-clinical, social, organizational, economic, technological,
and to improve the quality of life.

generally, all systems developed to solve a health problem could be drugs, medical devices, vaccines, procedures, and, generally, all systems developed to solve a health problem and to improve the quality of life.

Parmar and Chan [16] used HTA methodology in urologic oncology. As a result of the rapid development of new cancer therapies, it is important to have a decision-making tool that leads to the choice of the right therapy in a short period of time. In this study, HTA was used as an approach that could help to guide value-based decision-making. An HTA model was developed for the evaluation of generic pharmaceutical products. This tool allows us to compare, both qualitatively and economically, equivalent drug preparation. HTA was employed to evaluate a new health technology for the thyroglobulin assay in patients with differentiated thyroid cancer. The authors used the Dynamic AHP as an HTA tool to reach the goal [17]; this paper proved also the utility of combining HTA with other managerial approaches.

Another promising tool to improve the quality of healthcare processes is Six Sigma (SS) [18–21]. Initially introduced in the manufacturing sector, today, it is widely developed in the health sector. SS relies on the “Define, Measure, Analyze, Improve, Control” cycle (DMAIC), which is a five-step procedure related to quality management and process improvement that exploits both statistical and managerial tools. Through this problem-solving strategy with a fixed structure, it is possible to analyze a process in order to improve its performance reducing the “natural variability” and carry out the “systematic control” of the critical variables to obtain a better result. The procedure is divided into the following phases: defining the project goals and customer (internal and external) requirements, measuring the process to determine current performance, analyzing and defining the root cause(s) of relevant defects, improving the process by eliminating defect root causes, and controlling future process performance. For the first time, Bill Smith developed this methodology in 1986 with the aim of reducing product or process defects that did not satisfy customers [18, 22]. DMAIC is then a framework used to enable the team to define and achieve set objectives [1, 23, 24].

From literature studies, it stands out the success that the strength of SS is founded not only in the manufacturing field but also in the health sector, where the SS DMAIC approach has been applied, for example, to improve first aid processes [25] and in the paramedical services [26]. Mahesh et al. [27] demonstrated how to reduce patients’ waiting time to receive a specialist medical visit at the Out-Patient Department of Cardiology in a private hospital in the city of Bangalore, and El-Eid et al. [28] have confirmed SS as an efficient and effective management tool to improve the patient discharge process, reducing patient discharge time. As well, other studies confirmed the validity of the methodology [13, 29–33], also in combination with other methods such as the Agile [34]. Ricciardi et al. [12] analyzed the introduction of the Diagnostic Therapeutic Assistance Path (DTAP), employing Lean Thinking and SS methodology based on the DMAIC cycle. Furthermore, several studies show that the SS is often associated with Lean Thinking: this approach aims to improve services to meet customer needs by eliminating wastes and reducing costs [35–37]. The use of these methodologies has reported multiple benefits in healthcare; in fact, they have been used to improve clinical decision-making processes and to reduce the risk of healthcare-associated infections in surgery departments [38], while others have conducted studies to introduce prehospitalization to perform the necessary tests and examinations for hip and knee prosthetic surgery [29, 39].

The problem of healthcare infections is of great interest in many surgery departments, and it is an indicator of hospital efficiency, safety, and quality. Scotton et al. [40] conducted a study whose purpose was to analyze infections in patients after Salvage Laryngectomy (SL) and review the potential impact of the antibiotic prophylaxis adopted. The results showed that infection rates after SL were high, and univariate analysis demonstrated risk variables that had a significant correlation with infection, so the antibiotic regimen is probably ineffective. Other authors [41–48] presented an overview of current evidence-based best practices in the use of prophylactic antibiotics in head and neck cancer surgery; indeed, this type of patient is at high risk of developing complications after surgery. Thus, they reported that prophylactic antibiotics helped significantly reduce the risk of infection [49]. However, short four-dose antibiotic regimens for 24 hours are as effective as prolonged cycles, regardless of the complexity of the procedure [50–53]. In the same framework, the research of Egan et al. [54] discusses the use of the SS focusing on therapy with antimicrobial gentamicin, which requires good practice in selecting the dose and monitoring serum levels. They found a new dosage with a standardized sampling, a monitoring program, and a new timing of drug delivery that maximized local capacities. In light of the above-mentioned studies, it emerges the importance of choosing correct prophylactic antibiotics to manage patients appropriately after surgical interventions.

To this aim, in our recent study [55], SS was employed to compare the use of antibiotics in patients undergoing oral cancer surgery on bone tissue. Starting from the previous promising results, in this work, two antibiotics, ceftriaxone and the combination of cefazolin and clindamycin, are compared in order to understand which one reduces the postoperative length of hospital stay (LOS) for patients undergoing oral cavity cancer surgery on the bone tissue. In this study, it is taken into consideration the clinical factor because the two antibiotics are quite similar from a safety, legal, ethical, economic, and technological point of view. Six Sigma (SS) methodology is applied as a tool of HTA in order to achieve the aim. SS was used to analyze the influence of some clinical variables (ASA score, age, gender, oral hygiene, diabetes, and cardiovascular diseases) on the Critical to Quality (CTQ) (postoperative LOS). Patients’ postoperative LOS can be described as the duration of time after a patient’s surgery until the day of discharge.
The novelty of this new study is the use of the DMAIC cycle as an HTA tool including a modeling phase. This would enable healthcare providers to understand the performance of antibiotics, improving patients’ outcomes, reducing postoperative LOS and related costs, consequently, increasing patient safety, and improving the quality of care provided. After applying DMAIC, a modeling study was conducted through a multinomial linear regression; in particular, it was applied to obtain two models capable of predicting postoperative LOS for each antibiotic. In order to do this, we included the surgical variables that were considered in the previous study [55].

2. Materials and Statistical Tools

SS and subsequently the modeling phase were used to implement the HTA methodology. In detail, deploying the DMAIC cycle, characteristic of SS, means developing five phases:

(1) The Define phase identifies the customers and the objectives to be reached will be established allowing a team to identify the problem

(2) The Measure phase defines the main characteristics of the process and the parameters that will lead to improvement

(3) The Analyze phase is used to understand the influence of the collected variables on the CTQ or to evaluate the data collected in the previous phases of the study using various analytical tools available such as regression analysis, fishbone diagram, tree diagrams, and brainstorming

(4) The Improve phase employs all the previous analyses to design changes in a process and to improve the performance, i.e., introducing a new antibiotic protocol

(5) The Control phase is employed to monitor the whole process and, in this research, to compare the performance of the drugs

SS led the way for the development of the modeling phase, providing us with information about all the variables. Modeling allowed us to enrich the univariate analysis with a multivariate one and to implement a tool able to predict the postoperative LOS for each patient. These models will be very useful for both ward management and hospital management. Predicting the LOS of a patient determines a more efficient hospital bed organization, a better management of nurses and doctors on duty, and lastly, a cost reduction for hospitals. Thus, combining SS and modeling could be considered a valuable tool for HTA methodology.

In conclusion, the purpose of this paper is to assess the performance of two antibiotics, cefazolin plus clindamycin and ceftriaxone, through an HTA by using SS and modeling as a tool in the framework of oral cavity cancer surgery on bone tissues.

2.1. The Clinical Case Study. In this study, two groups of patients with oral cancer starting from the bone were analyzed: the first one was treated with ceftriaxone between 2006 and 2011, while the second one was treated with cefazolin and clindamycin between 2011 and 2019. The cefazolin group consisted of 54 patients, while the other by 51 patients. Oral cancer is the sixth most common cancer in the world [60] but the ones starting from the jaws are rare. The majority of the oral cancers affecting the bone derives from the epithelial quote of the oral mucosa, but there are also cancers that originally start from the bones, which are rare. Sarcomas are very rare tumors in the head and neck district, osteosarcoma being the most common of them [61]. They represent 1% of all the malignancies affecting the head and neck [62]. The incidence of sarcomas starting from the mandibles ranges from 4% to 10% [63]. In this study, we decided to analyze also those patients affected by ameloblastomas, which is not actually a malignant neoplasm. This choice is due to the fact that in the case of big ameloblastomas affecting the jaws, a big removal of tissue and reconstruction with the same surgical techniques used for patients affected by oral bone cancers are often required. The data was taken from printed medical records. Statistical tests, useful for analyses, were carried out with IBM SPSS.

For the collection of data, some inclusion and exclusion criteria were taken into consideration:

(i) All patients were included without exclusion due to medical history (gender, age, cardiovascular diseases, diabetes, oral hygiene, American Society of Anaesthesiologists (ASA) Score)

(ii) Patients with cancers starting from the bones or starting from the oral mucosa and then affecting the bone were included. We also included patients with ameloblastomas because of their osteolytic patterns

(iii) Patients treated in “day surgery” were excluded

(iv) Patients with too many missing data were not included because they would compromise the analysis

(v) Patients with a change of the antibiotic therapy during their recovery, because no evidence of efficacy, were not included in the analysis, but their number was recorded as it is a qualitative indicator of treatment failure

(vi) Patients allergic to cefazolin and clindamycin or ceftriaxone were excluded

As regards the Unit of Maxillofacial Surgery, the ward consists of 9 rooms with 22 beds for the patients and some more rooms for surgeons and nurses. The Operatory Block of the Department disposes of two operating rooms.

Oncological maxillofacial surgery is a branch of maxillofacial surgery which deals with the surgical approach to head and neck malignancies and the reconstruction of the lost tissues [64].

When no allergy was described, from 2006 to 2011, a postoperative antibiotic protocol with ceftriaxone was used. Since 2011, there has been a shift to the use of the association of cefazolin plus clindamycin as postoperative antibiotic prophylaxis.

2.2. The Development of the Six Sigma: The Define Phase. The purpose of the “Define” phase is to define a multidisciplinary workgroup and to divide the tasks for the analysis.
The team consists of clinicians from the Maxillofacial Department of the University Hospital “Federico II” of Naples, an economist, and biomedical engineers with experience in health management. The team was responsible for collecting and analyzing data of patients with oral cavity cancer considering the influence of some variables. The sample and the leader supervised and coordinated the study and interpretation of the data. A project diagram was created to define the problem to be solved:

(i) **Project Title.** Health Technology Assessment between two antibiotics in the context of Maxillofacial Surgery

(ii) **Question.** Investigation of the best antibiotics in the analyzed context

(iii) **Critical to Quality.** Postoperative LOS

(iv) **Target.** Realize corrective measures to reduce the CTQs

(v) **Deliverables.** The performance of cefazolin/clindamycin and ceftriaxone, the outcome of patients, reducing postoperative LOS, and the related costs

(vi) **Timeline:**
   1. Define: January 2010
   2. Measure: January 2010
   3. Analyze: January 2010
   4. Improve: January 2011
   5. Control: 2011–2018

(vii) **In Scope.** Oral cavity cancer surgery on bone tissues. Maxillofacial surgery in the University Hospital of Naples “Federico II”

(viii) **Out of Scope.** All the other structures and interventions and drugs

(ix) **Financial.** No funding to reach the target

(x) **Business Need.** Identifying the best antibiotic for the surgery under examination

2.3. **Dataset Description: The Measure Phase.** The data collected from the medical records at the Department of Maxillofacial Surgery were selected according to the inclusion and exclusion criteria. After applying the inclusion and exclusion criteria, the first sample of data concerned patients treated with ceftriaxone from 2006 to 2011 (45 patients), and the other sample of data (48 patients) was referred to patients treated with cefazolin and clindamycin from 2011 to 2019. The variables used to compare the two antibiotics were

(i) Gender

(ii) Age

(iii) American Society of Anaesthesiologists (ASA) Score

(iv) Quality of oral hygiene

(v) Diabetes

(vi) Cardiovascular diseases

Other variables were analyzed through univariate analysis in a previous study [55]; thus, they were included only in the modeling phase. Descriptive characteristics of the dataset were carried out for the postoperative LOS variables: the results for cefazolin/clindamycin were, respectively, an average of 16.51 days and a variance of 62.21. Instead, the results for ceftriaxone were an average of 9.75 days and a variance of 66.81.

We drew a histogram (Figure 1) showing the mean postoperative LOS of patients, measured in days, submitted to the administration of cefazolin/clindamycin according to each variable. The highest average LOS is for patients with a high ASA score, while the lowest is for patients with a low ASA score.

Figure 2 shows the distribution of mean postoperative LOS of patients who used ceftriaxone. Patients below the age of 51 have the highest mean LOS, whereas those without cardiovascular disease have the lowest mean LOS.

2.4. **Statistical Analysis: The Analyze Phase.** In Figure 3, patients’ pathway is shown from the arrival at the hospital to the discharge. They arrived at the hospital; then, if they receive a previous prehospitalization, they undergo surgery directly; otherwise, they are subjected to preoperative activities before surgery. Finally, if there are complications after the surgery, the patient undergoes postoperative activities; otherwise, they will be discharged after fewer days.

A Kolmogorov–Smirnov test showed a \( p \) value lower than 0.0001. In order to understand the variables that could influence the postoperative LOS in the ceftriaxone group, nonparametric tests were employed: Mann–Whitney and Kruskal–Wallis (only for age). In this case, some significant \( p \) values were found for age and ASA score while the \( p \) value of cardiovascular disease was almost significant (\( p \) value = 0.066) (Table 1).

A box diagram was developed and is shown in Figure 4, which clearly highlights the decrease in the ceftriaxone group of LOS, measured in days.

The Control phase allowed us to monitor and guarantee the sustainability of the long-term continuous improvement of the performance. Thus, the team identified the following actions:

(i) Periodic review meetings to evaluate the maxillofacial surgery process

(ii) Internal audit to verify the performance of antibiotics

(iii) Production of reports that highlight the trend of patients’ postoperative patients measured in days

After analyzing the data according to the DMAIC cycle, the modeling phase started by implementing the multiple linear regression. It is also known simply as multiple regression and is a statistical technique that uses several explanatory variables to predict the outcome of a response variable. The goal of multiple linear regression is to model the linear relationship between the explanatory (independent) variables and response (dependent) variables. In other words, multiple regression is the extension of ordinary least-squares (OLS) regression that involves more than one explanatory variable.
In this study, it was used to obtain a model capable of predicting the postoperative LOS for each patient undergoing oral cavity cancer surgery on the bone. In order to obtain the best models, we considered also the surgical variables that were studied in a previous research on the same topic [55]. Therefore, the considered variables in order

**Figure 1:** Mean postoperative LOS for each mode of variables regarding cefazolin/clindamycin.

**Figure 2:** Mean postoperative LOS for each mode of variables regarding ceftriaxone.

**Figure 3:** The flowchart of the hospitalization process for patients undergoing oncologic surgery at the Maxillofacial Department of the University Hospital of Naples "Federico II."

In this study, it was used to obtain a model capable of predicting the postoperative LOS for each patient undergoing oral cavity cancer surgery on the bone. In order to obtain the best models, we considered also the surgical variables that were studied in a previous research on the same topic [55]. Therefore, the considered variables in order
Table 1: The analysis of potential factors influencing postoperative LOS for the “ceftriaxone” group.

| Variable         | Category | N  | LOS (mean ± std. dev.) | p value |
|------------------|----------|----|------------------------|---------|
| Gender           | Men      | 25 | 9.04 ± 7.49            | 0.669   |
|                  | Women    | 23 | 10.40 ± 9.02           |         |
| Age              | <50      | 21 | 6.52 ± 5.33            |         |
|                  | 50< age <61 | 9  | 8.89 ± 6.92            | 0.013*  |
|                  | >60      | 18 | 13.94 ± 10.04          |         |
| ASA score        | Low      | 30 | 7.33 ± 5.84            | 0.007   |
|                  | High     | 18 | 13.78 ± 10.15          |         |
| Oral hygiene     | Low      | 30 | 8.00 ± 6.74            | 0.306   |
|                  | High     | 18 | 10.80 ± 9.00           |         |
| Diabetes         | No       | 42 | 9.19 ± 8.05            | 0.213   |
|                  | Yes      | 6  | 13.67 ± 9.46           |         |
| Cardiovascular   | No       | 27 | 8.15 ± 7.48            | 0.066   |
| disease          | Yes      | 21 | 11.81 ± 8.92           |         |

* Kruskal–Wallis test.

Figure 4: Boxplot of the mean postoperative LOS for “cefazolin/clindamycin” and “ceftriaxone” groups.

The results of the comparison between the two antibiotics through Mann–Whitney and Kruskal–Wallis tests with an alpha level of 0.05 are shown in Table 3. Overall, the difference in postoperative LOS between the cefazolin/clindamycin and ceftriaxone groups was statistically significant with a reduction of 40.9%. All tests were statistically significant among the mode of variables, except for older patients (>60 years with a p value of 0.117). The greatest reduction in postoperative LOS results in younger patients (<51 years with a reduction of 54.1%) and people with low oral hygiene (52.4%).

Table 4 shows the results of a study regarding the frequencies of each variable, obtained by performing a chi-square test. A statistically significant difference between the occurrences of cefazolin/clindamycin and ceftriaxone groups was obtained according to age, ASA score, and oral hygiene.

3.3. Combining Ss and Modeling. The statistical analysis was useful for the subsequent modeling phase. As mentioned in the introduction, in this phase, we also considered some surgical variables analyzed in a preceding paper [55]. For both antibiotic protocols, the multiple linear regression was implemented obtaining two predictive models whose equations are shown as follows:

\[ y_1 = \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \beta_5 x_5 + \beta_6 x_6 + \beta_7 x_7 + \beta_8 x_8 + \epsilon_1, \] (1)

\[ y_2 = \gamma_1 x_1 + \gamma_2 x_2 + \gamma_3 x_3 + \gamma_4 x_4 + \gamma_5 x_5 + \gamma_6 x_6 + \gamma_7 x_7 + \gamma_8 x_8 + \epsilon_2, \] (2)

where \( y_1 \) represents the LOS of patients treated with cefazolin/clindamycin, \( y_2 \) the LOS of patients treated with ceftriaxone, \( x_i \) the considered variables, \( \beta_i \) and \( \gamma_i \) the regression coefficients, and \( \epsilon_i \) the errors.

Before carrying out the regression analysis, it is necessary to verify, for both antibiotics, the hypotheses given in Table 5 which also contains references to the additional material provided in order to give more details on these verifications.
As shown in equations (1) and (2), not all variables were considered for both models. In particular, 8 variables were included for cefazolin/clindamycin (ASA score, diabetes, cardiovascular disease, tracheotomy, lymphadenectomy, infections, dehiscence, and flap) while 6 variables were included for ceftriaxone (ASA score, oral hygiene, diabetes, cardiovascular disease, lymphadenectomy, and flap). The exclusion criteria of variables in each model were as follows:

(i) Gender and age were excluded in order to obtain models based on clinical factors

(ii) Oral hygiene was excluded from the cefazolin/clindamycin model because it did not respect the "absence of multicollinearity" hypothesis; i.e., there was a dependency between it and the ASA score variable. Since ASA score had a lower p value in the previous analyses of DMAIC than oral hygiene, the latter was excluded.
(i) Infections and dehiscence were excluded from the ceftriaxone model because no patient has experienced them. Similarly, the tracheotomy variable was excluded because there was only one case and it was not enough.

Tables 6 and 7 show the regression coefficients, errors, and statistical significance obtained for each variable.

The results show that for cefazolin/clindamycin the ASA score is statistically significant and the flap is very close to the p value of 0.05. Similarly, for ceftriaxone the ASA score and the flap are variables that have a significant effect on LOS, as well as oral hygiene and lymphadenectomy.

A summary of the two models is given in Table 8. In particular, there are the coefficient of determination ($R^2$), the adjusted $R^2$, squared, and the standard error of the estimate.

Since the two models have a different number of predictors, in addition to the $R^2$, the adjusted $R^2$ has also been reported; it is a modified version of $R^2$, adjusted according to the number of predictors in the model. Although there are also other variables affecting LOS, the results obtained indicate that, for both antibiotics, about 82–89 percent of the variance in LOS is explained by the selected variables.

### 4. Discussion and Conclusion

Over the past few years, the healthcare sector has paid attention to cost increases, mainly due to the drop of refunds, and to improve the experience of patients. In this scenario, the HTA provides health leaders with a useful tool to improve the efficiency and effectiveness of clinical processes; this tool has become fundamental in healthcare due to the high amount of medical device patents that have been required in the last decades [65]. In the literature, some studies applied the HTA to support decision-making processes regarding the purchase of medical devices [66] or drug refund policies [67, 68], while only a few works present an application of the HTA for evaluating the introduction of new antibiotic prophylaxis. In this study, we tackled this issue by employing a combination of both SS and HTA. In particular, encouraged by the results achieved in previously published studies [7, 55], here we adapted the framework of the SS DMAIC cycle to build a tool that could support the HTA of a new antibiotic prophylaxis procedure for patients undergoing oral cancer surgery of the bone. The assessment has been made taking into account a healthcare key performance indicator, which is the postoperative LOS. Indeed, the LOS is a useful metric to determine the economic, organizational, and clinical impact of healthcare services. In this work, a multiple regression model has been integrated within the SS framework to investigate the relationships between a prolonged LOS and the prophylaxis procedure in order to determine the impact of the introduction of a new antibiotic on the hospital stay. When framed into the Improve phase of the SS DMAIC cycle, the regression model helped in determining the effect of the new antibiotic prophylaxis on the postoperative LOS and enabled a comparison between the two antibiotics, thus providing an additional informative tool to support the decision-making process, in accordance with our previous works [7, 55].

The results obtained from the comparative statistical analysis (Table 3) showed a 41% reduction in the LOS for patients treated with ceftriaxone compared to those treated with cefazolin/clindamycin, with the highest decrease achieved among younger patients (−54.1%). This could be due to the better response of younger patients toward the performed surgical procedure, as opposed to older patients, whose surgical intervention can be influenced by possible comorbidities and other variables, in accordance with the literature [69, 70]. The modeling phase with the two regression models (Tables 6 and 7) enabled the identification of the variables, among demographic, clinical, and surgical ones as considered in a previous study [55], which influence the postoperative LOS the most and provided promising tools for the prediction of the LOS in patients undergoing oral cavity cancer surgery on the bone who are treated with cefazolin/clindamycin or with ceftriaxone. Of note, during the whole study’s range of time, the choice of the antibiotics was completely independent.
of the research. Indeed, the antibiotic to be administered was defined by the hospital’s protocols which change the antibiotic choice in 2011 according to the new trends of therapy described in the medical literature.

In summary, the proposed approach confirmed the value of combining both the SS DMAIC approach and modeling, which can serve as a tool to support HTA processes for understanding the optimal therapeutic approach.

In conclusion, this HTA study confirmed and further extended the results achieved and presented in the literature which considered the ceftriaxone as the best option for patients undergoing oral cancer surgery on bone tissue [55] and provides the health policy with two important results: the antibiotic which reduces the postoperative LOS and two models which predict it. Succeeding in predicting the postoperative LOS of a patient could lead to many benefits for both the hospital and patients. Indeed, the hospital could better manage all its resources, reduce waste and costs, and improve the understanding of patients’ needs, which are all aims of an SS project; meanwhile, the patients could experience a better quality of care and a lower LOS.

The evaluation of antibiotic performance is an important topic, as it is linked to healthcare-associated infections in hospitals, as evidenced by studies in the literature. This paper evaluates the performance of antibiotics considering the most important variables in the maxillofacial area. In addition, the DMAIC approach implies a positive advantage, giving support to the medical staff in the decision-making process of antibiotic administration, reducing the gap between practice and theory. Therefore, the reduction of postoperative LOS and the rate of infections of patients undergoing oral cavity cancer surgery benefit both the hospital and patients: patients satisfied in terms of a few days of hospitalization and effective and efficient therapy, while the hospital has more available beds and saves costs of managing patients with complications.

**Abbreviations**

ASA: American Society of Anaesthesiologists  
CTQ: Critical to quality  
DMAIC: Define, Measure, Analyze, Improve, Control  
LOS: Length of hospital stay  
SPSS: Statistical Software for the Social Sciences  
SS: Six Sigma.

**Data Availability**

Data are not present in a publicly accessible repository. Data could be made available upon reasonable request to the authors.

**Conflicts of Interest**

The authors declare they have no conflicts of interest.

**Authors’ Contributions**

Alfonso Maria Ponsiglione, Carlo Ricciardi, Arianna Scala, Giovanni Dell’Aversana Orabona and Giovanni Improta contributed equally to this work.

**Supplementary Materials**

Details on the multiple regression model assumptions check (as briefly summarized in Table 5 of the manuscript) are reported in the attached Supplementary Material file. (Supplementary Materials)

**References**

[1] S. Akifuddin and F. Khatoon, “Reduction of complications of local anaesthesia in dental healthcare setups by application of the six sigma methodology: a statistical quality improvement technique,” *Journal of Clinical and Diagnostic Research: Journal of Clinical and Diagnostic Research*, vol. 9, no. 12, pp. 2C34–38, 2015.

[2] S. Domínguez and M. C. Carnero, “Fuzzy multicriteria modelling of decision making in the renewal of healthcare technologies,” *Mathematics*, vol. 8, no. 6, 2020.

[3] C. Ricciardi, A. M. Ponsiglione, G. Converso, I. Santalucia, M. Triassi, and G. Improta, “Implementation and validation of a new method to model voluntary departures from emergency departments,” *Mathematical Biosciences and Engineering*, vol. 18, no. 1, pp. 253–273, 2021.

[4] A. Scala, A. M. Ponsiglione, I. Loperto et al., “Lean six sigma approach for reducing length of hospital stay for patients with femur fracture in a university hospital,” *International Journal of Environmental Research and Public Health*, vol. 18, no. 6, 2021.

[5] G. Improta, A. M. Ponsiglione, G. Parente et al., “Evaluation of medical training courses satisfaction: qualitative analysis and analytic hierarchy process,” in *Proceedings of the 8th European Medical and Biological Engineering Conference*, T. Jarm, A. Cvetkoska, S. K. Mahnič, and D. Miklavec, Eds., Springer International Publishing, Portorož, Slovenia, pp. 518–526, November 2020.

[6] M. J. Glover, E. Jones, K. L. Masconi, M. J. Sweeting, and S. G. Thompson, “Discrete event simulation for decision modeling in health care: lessons from abdominal aortic aneurysm screening,” *Medical Decision Making*, vol. 38, no. 4, pp. 439–451, 2018.

[7] A. M. Ponsiglione, C. Ricciardi, G. Improta et al., “A Six Sigma DMAIC methodology as a support tool for Health Technology Assessment of two antibiotics,” *Mathematical Biosciences and Engineering*, vol. 18, no. 4, pp. 3469–3490, 2021.

[8] A. Glaize, A. Dueñas, C. D. Martinelly, and I. Fagnou, “Healthcare decision-making applications using multicriteria decision analysis: a scoping review,” *Journal of Multi-Criteria Decision Analysis*, vol. 26, no. 1–2, pp. 62–83, 2019.

[9] G. D’Addio, C. Ricciardi, G. Improta, P. Bifulco, and M. Cesarelli, “Feasibility of machine learning in predicting features related to congenital nystagmus,” in *Proceedings of the Mediterranean Conference on Medical and Biological Engineering and Computing*, Springer, Coimbra, Portugal, September 2019.

[10] C. Ricciardi, V. Cantoni, G. Improta et al., “Application of data mining in a cohort of Italian subjects undergoing myocardial perfusion imaging at an academic medical center,” *Computer Methods and Programs in Biomedicine*, vol. 189, 2020.

[11] C. Ricciardi, K. J. Edmunds, M. Recenti et al., “Assessing cardiovascular risks from a mid-thigh CT image: a tree-based machine learning approach using radiodensitometric distributions,” *Scientific Reports*, vol. 10, no. 1, pp. 1–13, 2020.
[12] C. Ricciardi, A. Fiorillo, A. S. Valente et al., “Lean Six Sigma approach to reduce LOS through a diagnostic-therapeutic-assistance path at A,” O.R.N. A. Cardarelli. The TQM Journal, vol. 31, no. 5, pp. 657–672, 2019.

[13] C. Ricciardi, G. Balato, M. Romano, I. Santalucia, M. Cesarelli, and G. Improta, “Fast track surgery for knee replacement surgery: a lean six sigma approach,” TQM Journal, vol. 32, no. 3, 2020.

[14] R. N. Battista and M. J. Hodge, “The evolving paradigm of health technology assessment: reflections for the millennium,” Canadian Medical Association Journal: Canadian Medical Association Journal, vol. 160, no. 10, pp. 1464–1467, 1999.

[15] C. Favaretti, A. Cicchetti, G. Guerrera, M. Marchetti, and W. Ricciardi, “Health technology assessment in Italy,” International Journal of Technology Assessment in Health Care, vol. 25, no. Suppl 1, pp. 127–133, 2009.

[16] A. Parmar and K. K. W. Chan, “Health technology assessment methodology in metastatic renal cell carcinoma,” Nature Reviews Urology, vol. 17, no. 1, pp. 3–5, 2020.

[17] C. Ricciardi, G. Balato, M. A. Russo, and M. Triassi, “Health technology assessment (HTA) of optoelectronic biosensors for oncology by analytic hierarchy process (AHP) and Likert scale,” BMC Medical Research Methodology, vol. 19, no. 1, 2019.

[18] J. Antony, P. Palusk, S. Gupta, D. Mishra, and P. Barach, “Six Sigma in healthcare: a systematic review of the literature,” International Journal of Quality & Reliability Management, vol. 35, no. 5, pp. 1075–1092, 2018.

[19] R. M. Alhamali, “Success factors and benefits of six sigma implementation in hospitals: a systematic review,” Business and Management Studies, vol. 5, no. 3, pp. 1–10, 2019.

[20] T. T. Allen, S.-H. Tseng, K. Swanson, and M. A. McClay, “Improving the hospital discharge process with six sigma methodology and factor Analysis,” International Journal for Quality Research, vol. 30, no. 4, pp. 373–384, 2017.

[21] G. Improta, C. Ricciardi, A. Borrelli, A. D’alessandro, G. Guizzi, C. Ricciardi et al., “Agile six sigma in clinical laboratories: a six sigma concept,” International Journal of Environmental Research and Public Health, vol. 19, no. 1, pp. 1–20, 2016.

[22] G. Improta, C. Ricciardi, G. Balato, M. A. Barghash, N. Haddad et al., “Using six sigma DMAIC methodology and discrete event simulation to reduce patient discharge time in king hussein cancer center,” Journal of Healthcare Engineering, vol. 2018, Article ID 3832151, 18 pages, 2018.

[23] V. Sawalakhke, S. V. Deshmukh, and R. R. Lakhe, Evaluating Performance of Testing Laboratory Using Six Sigma 1 Pranil, 2016.

[24] M. A. O. Barrios and H. F. Jiménez, “Use of six sigma methodology to reduce appointment lead-time in obstetrics outpatient department,” Journal of Medical Systems, vol. 40, no. 10, p. 220, 2016.

[25] A. George, A. M. Joseph, S. Kolencherry et al., “Application of six sigma dmaic methodology to reduce medication errors in a major trauma care centre in india,” Indian Journal Of Pharmacy Practice, vol. 11, no. 4, pp. 182–187, 2018.

[26] M. Fieri, N. F. Ranney, E. B. Schroeder, E. M. A. Van, and A. H. Stone, “Analysis and improvement of patient turn-around time in an Emergency Department,” in Proceedings of the 2010 IEEE Systems and Information Engineering Design Symposium, pp. 239–244, Charlottesville, VA, USA, April 2010.

[27] A. A. Baddour and H. A. Saleh, “Use six sigma approach to improve healthcare workers safety,” International Journal of Pure and Applied Sciences and Technology, vol. 18, no. 1, 2013.

[28] B. P. Mahesh, B. Soragaon, and A. R. Annigeri, “Reduction of patient wait time at a multi-speciality hospital using DMAIC methodology and factor Analysis,” International Journal of Engineering & Technology, vol. 7, no. 4, pp. 309–312, 2018.

[29] G. R. E. El-Eid, R. Kaddoum, H. Tamim, and E. A. Hitti, “Improving hospital discharge time: a successful implementation of six sigma methodology,” Medicine, vol. 94, no. 12, 2015.

[30] G. Improta, G. Balato, M. Romano et al., “Improving performances of the knee replacement surgery process by applying DMAIC principles,” Journal of Evaluation in Clinical Practice, vol. 23, no. 6, pp. 1401–1407, 2017.

[31] G. Improta, G. Balato, C. Ricciardi et al., “Lean Six Sigma in healthcare: fast track surgery for patients undergoing prosthetic hip replacement surgery,” The TQM Journal, vol. 31, no. 3, 2019.

[32] A. A. Kuwaiti and A. V. Subbarayalu, “Reducing patients’ falls rate in an academic medical center (AMC) using six sigma “DMAIC” approach,” International Journal of Health Care Quality Assurance, vol. 30, no. 4, pp. 373–384, 2017.

[33] A. A. Kuwaiti and A. V. Subbarayalu, “Reducing hospital-acquired infection rate using the six sigma DMAIC approach,” Saudi Journal of Medicine & Medical Sciences, vol. 5, no. 3, pp. 260–266, 2017.

[34] A. Al Kuwaiti, “Application OF six sigma methodology to reduce medication errors IN the outpatient pharmacy unit: a case study from the king fahd university hospital, Saudi Arabia,” International Journal for Quality Research, vol. 10, no. 2, 2016.

[35] G. Improta, G. Guizzi, C. Ricciardi et al., “Agile six sigma in healthcare: case study at santobono pediatric hospital,” International Journal of Environmental Research and Public Health, vol. 17, no. 3, 2020.

[36] G. Improta, C. Ricciardi, A. Borrelli, A. D’alessandro, C. Verdoliva, and M. Cesarelli, “The application of six sigma to reduce the pre-operative length of hospital stay at the hospital Antonio Cardarelli,” International Journal of Lean Six Sigma, vol. 11, no. 3, 2019.

[37] J. Kalra and A. Kopargaonkar, “Quality improvement in clinical laboratories: a six sigma concept,” Pathology and Laboratory Medicine, vol. 1, no. 1, pp. 11–20, 2016.

[38] H. D. Koning, J. P. S. Verver, J. V. D. Heuvel, S. Bisgaard, and R. J. M. M. Does, “Lean six sigma in healthcare: Official Publication of the National Association for Healthcare Quality, vol. 28, no. 2, pp. 4–11, 2006.

[39] E. Montella, M. V. D. Cicco, A. Ferraro et al., “The application of Lean Six Sigma methodology to reduce the risk of healthcare-associated infections in surgery departments,” Journal of Evaluation in Clinical Practice, vol. 23, no. 3, pp. 530–539, 2017.

[40] G. Improta, G. Balato, M. Romano et al., “Lean Six Sigma: a new approach to the management of patients undergoing prosthetic hip replacement surgery,” Journal of Evaluation in Clinical Practice, vol. 21, no. 4, pp. 662–672, 2015.

[41] W. Scotton, R. Cobb, L. Pang et al., “Post-operative wound assistance path at A,” O.R.N. A. Cardarelli. The TQM Journal, vol. 31, no. 5, pp. 657–672, 2019.

[42] S.-C. Chang, M. Jenab, J. E. Heck et al., “Diet and the risk of head and neck cancer: a pooled analysis in the INHANCE
Journal of Healthcare Engineering

M. Pipan, “Quality improvement methodologies: PDCA cycle, RADAR matrix, DMAIC and DFSS,” 2010.

T. F. S. Cunha, T. A. M. Soares, C. M. Z. F. Ribeiro, J. A. D. B. Almeida, S. M. Miguel, and D. A. E. D. B. C. André, “Risk factors for surgical site infection in cervico-facial oncological surgery,” Journal of Cranio-Maxillofacial Surgery, vol. 40, no. 5, pp. 443–448, 2012.

M. Hashibe, P. Brennan, S. Chuang et al., “Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the INHANCE consortium. Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research,” cosponsored by the American Society of Preventive Oncology, vol. 18, no. 2, pp. 541–550, 2009.

A. R. Jethwa and S. S. Khariwala, “Tobacco-related carcinogenesis in head and neck cancer,” Cancer and Metastasis Reviews, vol. 36, no. 3, pp. 411–423, 2017.

N. Penel, C. Fournier, D. Lefebvre, and J. L. Lefebvre, “Multivariate analysis of risk factors for wound infection in head and neck squamous cell carcinoma surgery with opening of mucosa. Study of 260 surgical procedures,” Oral Oncology, vol. 41, no. 3, pp. 294–303, 2005.

L. Radoï and D. Luce, “A review of risk factors for oral cavity cancer: the importance of a standardized case definition,” Community Dentistry and Oral Epidemiology, vol. 41, no. 2, pp. e78–91, 2013.

R. Saulle, L. Semyonov, A. Mannocci et al., “Human papillomavirus and cancerous diseases of the head and neck: a systematic review and meta-analysis,” Oral Diseases, vol. 21, no. 4, pp. 417–431, 2015.

K. Loftus, T. Tilley, J. Hoffman, E. Bradburn, and E. Harvey, “Use of Six Sigma strategies to pull the line on central line-associated bloodstream infections in a neurotrauma intensive care unit,” Journal of Trauma Nursing, vol. 22, no. 2, pp. 78–86, 2015.

R. Simo and G. French, “The use of prophylactic antibiotics in head and neck oncological surgery,” Current Opinion in Otolaryngology & Head and Neck Surgery, vol. 14, no. 2, pp. 55–61, 2006.

M. Garnier, C. Blayau, J.-P. Fulgencio et al., “[Rational approach of antibioprophylaxis: systematic review in ENT cancer surgery],” Annales Françaises d’Anesthésie et de Réanimation, vol. 32, no. 5, pp. 315–324, 2013.

Y. M. Haidar, P. B. Tripathi, T. Tjoa et al., “Antibiotic prophylaxis in clean-contaminated head and neck cases with microvascular free flap reconstruction: a systematic review and meta-analysis,” Head & Neck, vol. 40, no. 2, pp. 417–427, 2018.

J. T. Johnson, L. V. Victor, E. N. Myers, R. R. Mudar, P. B. Thearle, and W. F. Diven, “Efficacy of two third-generation cephalosporins in prophylaxis for head and neck surgery,” Archives of Otolaryngology, vol. 110, no. 4, pp. 224–227, 1984.

S. Egan, P. G. Murphy, I. P. Fennell et al., “Using Six Sigma to improve once daily gentamicin dosing and therapeutic drug monitoring performance,” BMJ Quality & Safety, vol. 21, no. 12, pp. 1042–1051, 2012.

C. Ricciardi, A. Sorrentino, G. Improta et al., “A health technology assessment between two pharmacological therapies through Six Sigma: the case study of bone cancer,” The TQM Journal, vol. 32, no. 6, 2020.

M. Pipan, “Quality improvement methodologies: PDCA cycle, RADAR matrix, DMAIC and DFSS,” 2010.

C. B. Mahesh, B. K. Ramakant, and V. S. Jagadeesh, “The prevalence of inducible and constitutive clindamycin resistance among the nasal isolates of staphylococci,” Journal of Clinical and Diagnostic Research: Journal of Clinical and Diagnostic Research, vol. 7, no. 8, pp. 1620–1622, 2013.

L. Lazzarini, M. Brunello, E. Padula, and F. D. Lalla, “Prophylaxis with cefazolin plus clindamycin in clean-contaminated maxillofacial surgery,” Journal of Oral and Maxillofacial Surgery: Official Journal of the American Association of Oral and Maxillofacial Surgeons, vol. 62, no. 5, pp. 567–570, 2004.

J. M. Heit, M. R. Stevens, and K. Jeffords, “Comparison of ceftriaxone with penicillin for antibiotic prophylaxis for compound mandible fractures,” Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology & Endodontology, vol. 83, no. 4, pp. 423–426, 1997.

K. Dhanuthai, S. Rojanawatsirivej, W. Thosaporn et al., “Oral cancer: a multicenter study,” Medicina Oral, Patologia Oral y Cirugía Bucal, vol. 23, no. 1, pp. e23–e29, 2018.

I. Petrovic, Z. U. Ahmed, A. Hay et al., “Sarcomas of the mandible,” Journal of Surgical Oncology, vol. 120, no. 2, pp. 109–116, 2019.

T. D. Shellenberger and E. M. Sturgis, “Sarcomas of the head and neck region,” Current Oncology Reports, vol. 11, no. 2, pp. 135–142, 2009.

A. Ketabchi, N. Kalavrezos, and L. Newman, “Sarcomas of the head and neck: a 10-year retrospective of 25 patients to evaluate treatment modalities, function and survival,” British Journal of Oral and Maxillofacial Surgery, vol. 49, no. 2, pp. 116–120, 2011.

S. Lester and W.-Y. Yang, “Principles and management of head and neck cancer,” Surgery - Oxford International Edition, vol. 33, no. 12, pp. 620–626, 2015.

L. Pecchia, N. Pallikarakis, R. Magiarevic, and E. Iadanza, “Health technology assessment and biomedical engineering: global trends, gaps and opportunities,” Medical Engineering & Physics, vol. 72, pp. 19–26, 2019.

G. Improta, M. A. Russo, M. Triassi, G. Converso, T. Murino, and L. C. Santillo, “Use of the AHP methodology in system dynamics: modelling and simulation for health technology assessments to determine the correct prosthesis choice for hernia diseases,” Mathematical Biosciences, vol. 299, pp. 19–27, 2018.

E. Y. Bae, J. M. Hong, H. Y. Kwon et al., “Eight-year experience of using HTA in drug reimbursement: South Korea,” Health Policy, vol. 120, no. 6, pp. 612–620, 2016.

L. Maynou and J. Cairns, “What is driving HTA decision-making? Evidence from cancer drug reimbursement decisions from 6 European countries,” Health Policy, vol. 123, no. 2, pp. 130–139, 2019.

M. Shayne, E. Kulakova, M. S. Poniewierski et al., “Risk factors for in-hospital mortality and prolonged length of stay in older patients with solid tumor malignancies,” Journal of Geriatric Oncology, vol. 4, no. 4, pp. 310–318, 2013.

R. Grossman, D. Mukherjee, D. C. Chang et al., “Preoperative Charlson comorbidity score predicts postoperative outcomes among older intracranial meningioma patients,” World Neurosurgery, vol. 75, no. 2, pp. 279–285, 2011.