**OBJECTIVES/AIMS:** The aim of this study was to investigate the microbial cultures collected in the years 2013–2014 at the cranio-maxillofacial department and outpatient clinic to analyse optimisation of the treatment cost of the bacterial infections and present the results.

**DESIGN AND SETTING:** We analysed 485 cultures from 263 patients, of which 77.28% consisted of Gram-positive bacteria. On the basis of the antibiotic efficacy, antibiotic price and the cost of entire treatment during hospitalisation, the most useful antimicrobial agents for the most common pathogens were selected.

**RESULTS:** The most frequently collected material was pus. The most common pathogens were found to be the *Staphylococcus epidermidis* (18%), *Streptococcus mitis* and *Str. oralis* (14%) and *S. aureus* (6.5%).

**DISCUSSION:** The most frequently isolated bacteria in other studies were the *Streptococcus* strain. Other authors showed that ceftriaxone is the most cost efficient agent. The use of postoperative antibiotic prophylaxis remains controversial.

**CONCLUSION:** The results of this study suggest that the most useful antibiotics for therapy, from the perspective of the cost minimisation, were gentamycin, trimethoprim with sulfamethoxazole and vancomycin.

**INTRODUCTION**
Recommendations on the administration of antibiotics as perioperative prevention has been elaborated for the Ministry of Health, the study do not provide a detailed review of maxillofacial surgical procedures, focusing primarily on ear nose throat (ENT) surgery. There are no pharmacoeconomic analyses, which look into the medications used in maxillofacial surgery.

The growing antibiotic resistance forces us to elaborate well-grounded and economically viable criteria pertaining to the use of antimicrobials. Antibiotics are often prescribed in a manner that is schematic and unreasonable (on patient’s request), particularly, in viral infections or fever of unknown aetiology, which results in greater number of antibiotic-resistant bacterial strains and multidrug-resistant organisms. Multiple drug resistance is a significant problem, where a given microorganism becomes resistant to several groups of antibiotics. Apart from the rational use of antibiotics, it is also of key importance to adhere to an appropriate dosing schedule. In order for the treatment to be efficacious, one has to determine the aetiology involved and examine the antibiotic sensitivity of the microorganism in question.

The aim of the study was to present the results of cost minimisation analysis with reference to bacterial infections based on microbial cultures collected in the years 2013–2014 at the cranio-maxillofacial department and outpatient clinic.

**MATERIALS AND METHODS**
In the period of 1 January 2013–31 December 2014, a total number of 485 bacterial and fungal strains were cultured from 263 patients (112 females and 151 males; Table 1) treated at the Department of Cranio-Maxillofacial surgery and outpatient maxillofacial clinic. The patients were aged 10–79 (mean age: 41.3) years. The material collected for studies was primarily pus from submandibular and submental abscesses (55%), maxillary sinus swabs from sinusitis (12.5%), cutaneous fistula from submandibular regions (10%), and wound swabs from various facial regions (6%) as well as bone swabs from mandible (4%). All the microbiological samples were analysed in the bacteriological unit of the Central Laboratory at the SPSK-M. First, the Gram-stained bacteriological preparations were made. Fungi of the genus Candida were identified by means of Candida ID bioMerieux chromogenic plates (BIOMERIEUX, Marcy-l’Etoile, France) and the Auxacolor 2 test by Bio-Rad Laboratories Inc. (Hercules, CA, USA). Antibiograms were prepared using VITEK 2 compact bioMerieux analyser (BIOMERIEUX). In the automatic method, antibiograms were made with a Vitek 2 compact analyser using AST-P 534 and AST-P-S33 cards for other streptococi, AST-P 536 for staphylococi, and AST-N 019 AST-N022 for Gram-negative bacteria. The cards, AST-P-S86, AST-P-S76 and ST01, were used for streptococi, AST-P-S80 for staphylococi, whereas AST-N-894, AST-N259, AST-N93 and AST-N260 were used for Gram-negative bacteria. Antibiogram interpretation concerning the disk method is as following: susceptible, semisusceptible and of resistance. The antibiograms performed on cards were following: susceptible, semisusceptible and resistant; and it is defined as minimum inhibitory concentration, the lowest antibiotic concentration that can inhibit the growth of a given microorganism.

Gram-positive and Gram-negative bacteria were compared for their sensitivity to nine antimicrobial agents. The results achieved were subjected to the Fisher test statistical analysis, with P < 0.05. The one-way analysis of variance with Dunnett’s post hoc test was carried out with the use of Pearson’s χ² test. GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego, CA, USA, was used for the purpose.

A series of calculations were performed to determine the antibiotics that had been the most beneficial in empirical treatment of conditions caused by the most common pathogens. Antibiotic efficacy, antibiotic price and the cost of entire treatment during hospitalisation were considered. The following mathematical model was elaborated for calculations.

\[
7\left(\prod_{k=1}^{l} p_{1} + \prod_{k=1}^{l} p_{2}\right) + 3\left(\prod_{k=1}^{l} p_{1} + 350r\right)
\]

s—percentage of bacteria sensitive to the antibiotic, \(p_{1}\)—price of empirical antibiotic therapy, \(p_{2}\)—price of targeted antibiotic therapy, \(r\)—percentage
of bacteria resistant to the antibiotic and 350 PLN—gross cost of patient day (when in hospital).

Criteria for the cost minimisation analysis

(1) Cost of empirical antibiotic therapy involving a sensitive bacterial strain.
(2) Cost of 3-day-long empirical antibiotic therapy involving a resistant bacterial strain.
(3) Cost of vancomycin-targeted treatment in drug-resistant patients.
(4) Total cost of 3-day-long empirical therapy in drug-resistant patients, followed by the 7-day-long targeted treatment.
(5) Total treatment costs for drug-sensitive and drug-resistant patients.
(6) The result that was extrapolated for a single patient.

The cost minimisation analysis was carried out for the prevalent bacteria isolated in 2013 and 2014 at the Department of Cranio-Maxillofacial Surgery at the maxillofacial outpatient clinic. The dominant strains were *S. epidermidis*, *Streptococcus mitis* and *Str. oralis* as well as *S. aureus*.

**RESULTS**

In 2013–2014 (Table 2), the most prevalent strain among the isolated Gram-positive bacteria was *Staphylococcus epidermidis*, totalling 48 strains (19.1%) in 2013 and 40 strains (17.2%) in 2014. *Str. mitis* and *Str. oralis* were second, constituting 37 strains (14.7%) of the cultured strains in 2013 and 30 strains (12.9%) in 2014 ($P = 0.24264$).

Regarding the Gram-negative bacteria in the years 2013–2014, 19 were *Klebsiella pneumoniae* strains (3.9%), 17 *Escherichia coli* strains (3.5%) and 14 were *Haemophilus* strains (2.9%). In the final 2 years, there was also a decrease in the number of the *Enterobacteriaceae* rods cultured, totalling seven strains (2.8%) in 2013 and it was five strains (2.15%) in 2014 ($P = 0.24264$).

In our studies, gentamycin showed statistically significant stronger effect than oxacillin (odds ratio (OR) = 3.05, $P = 0.003$), tobramycin (OR = 4.753, $P < 0.0001$) and penicillin (OR = 27.41, $P < 0.0001$). In contrast, clindamycin, tetracycline and erythromycin are weaker than gentamycin by $0.2694 (P < 0.0001)$, $0.1734 (P < 0.0001)$ and $0.1638 (P < 0.0001)$ respectively.

From the perspective of cost minimisation, the most advantageous antibacterial drug, due to its high efficiency towards *Str. mitis* and *Str. oralis*, turns out to be vancomycin (Figure 1), in which case the total costs of the therapy of 100 patients amount to 21,980 PLN, compared to the 58,090 PLN for ceftriaxone. This is because resistant bacteria will have to be

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**Table 1.** Characterisation of bacteria isolates

| Number of pathogens | Number of patients | Total number of cultured strains |
|---------------------|--------------------|---------------------------------|
| 1                   | 111                | 111                             |
| 2                   | 101                | 202                             |
| 3                   | 32                 | 96                              |
| 4                   | 19                 | 76                              |
| Total               | 263                | 485                             |

**Table 2.** Antibiotic sensitivity of *S. aureus*, *S. epidermidis*, *Str. mitis* and *Str. oralis*

| Trimethoprim/ sulfamethoxazole | Vancomycin | Clindamycin | Gentamycin | Tetracyclin | Erythromycin | Teicoplanin | Ampicillin | Penicillin G | Ceftriaxone |
|-------------------------------|------------|-------------|------------|-------------|--------------|-------------|------------|--------------|-------------|
| S. epidermidis 88 strains (19%) |            |             |            |             |              |             |            |              |             |
| Drug sensitivity              |            |             |            |             |              |             |            |              |             |
| Number                        | 81         | 88          | 49         | 80          | 42           | 46          | NA         | NA           | NA          |
| %                             | 92         | 100         | 56         | 91          | 48           | 52          | NA         | NA           | NA          |
| Drug resistance               |            |             |            |             |              |             |            |              |             |
| Number                        | 3          | 0           | 19         | 2           | 23           | 42          | NA         | NA           | NA          |
| %                             | 8          | 0           | 44         | 9           | 52           | 48          | NA         | NA           | NA          |
| S. mitis and Str. oralis 67 strains (13.8%) |            |             |            |             |              |             |            |              |             |
| Drug sensitivity              |            |             |            |             |              |             |            |              |             |
| Number                        | NA         | 66          | 40         | NA          | NA           | NA          | NA         | 35           | 48          |
| %                             | NA         | 99          | 60         | NA          | NA           | NA          | NA         | 52           | 72          |
| Drug resistance               |            |             |            |             |              |             |            |              |             |
| Number                        | NA         | 1           | 27         | NA          | NA           | NA          | NA         | 32           | 19          |
| %                             | NA         | 1           | 40         | NA          | NA           | NA          | NA         | 48           | 28          |
| S. aureus 31 strains (6.4%)   |            |             |            |             |              |             |            |              |             |
| Drug sensitivity              |            |             |            |             |              |             |            |              |             |
| Number                        | 29         | 31          | 27         | 29          | 23           | 26          | 31         | NA           | NA          |
| %                             | 94         | 100         | 87         | 94          | 74           | 84          | 100        | NA           | NA          |
| Drug resistance               |            |             |            |             |              |             |            |              |             |
| Number                        | 2          | 0           | 4          | 2           | 8            | 5           | 0          | NA           | NA          |
| %                             | 6          | 0           | 13         | 6           | 26           | 16          | 0          | NA           | NA          |

**Treatment cost (PLN)**

| Route of administration | i.v. | i.v. | i.v. | i.v. | p.o. | p.o. | i.v. | i.v. | i.v. | i.v. |
|-------------------------|------|------|------|------|------|------|------|------|------|------|
| 1 day                   | 8.3  | 31.4 | 23.26| 3.02 | 6.32 | 5.96 | 172.37| 12.12| 13.42| 13.42|
| 7 days                  | 58.1 | 219.8| 162.82| 21.14| 44.24| 41.72| 1206.59| 84.84| 93.94| 93.94|
| 10 days                 | 83   | 314  | 232.6| 30.2 | 63.2 | 59.6 | 1723.7| 121.2| 134.2| 134.2|
| 14 days                 | 116.2| 439.6| 325.64| 42.28| 88.48| 83.44| 2413.18| 169.68| 187.88| 187.88|

Abbreviations: i.v., intravenous; NA, not available; p.o, per os. oral administration.
treated with vancomycin. In contrast, gentamycin turns out to be the most advantageous against *S. epidermidis* (Figure 2), where the cost of the therapy is 8,402.6 PLN, whereas for trimethoprim/sulfamethoxazole, it is 15,084.5 PLN. The cost of treatment of *S. aureus* infections is the most beneficial with gentamycin (Figure 3), as it amounts to 15,353.16 PLN; and for trimethoprim/sulfamethoxazole treatment, it is 18,826.84 PLN.

**Figure 1.** The graph presents the costs of treatment of the infection caused by *Streptococcus mitis* and *Str. oralis* with particular antibiotics.

**Figure 2.** The graph presents the costs of treatment of the infection of *Staphylococcus epidermidis* with particular antibiotics.
fractures.15 Similar observations were made by Andreasen
complications compared to the 5-day prophylaxis in all types of
that 1-day prophylaxis is suf
for the period of 1–
fractures. The patients were given amoxicillin with clavulanic acid
S. epidermidis
strain.
that the most frequently isolated bacteria were the
controlled study concerning the application of perioperative
Switzerland carried out randomised, double-blinded placebo-
important source of infections of implants. 13,14 Zix
Scopus. This was also presented in our study.
Similar results were obtained by Ru et al.,8 who have also shown
the most frequently isolated bacteria were the Streptococcus
strain. S. epidermidis was detected in 19% patients. This strain is a
commensal bacterium colonising skin and mucous. It might also
de be due to swab contamination; however, S. epidermidis produces
many virulence factors and forms biofilm, and was isolated in
sinusitis and is now considered as one of the major source of
nosocomial infections.9–12 Furthermore, S. epidermidis are the
important source of infections of implants.13,14 Zix et al. in
Switzerland carried out randomised, double-blinded placebo-
controlled study concerning the application of perioperative
therapy with antibiotics in 62 patients with orbit fractures and
in 94 patients with maxillary and orbital–maxillary–zygomatic
fractures. The patients were given amoxicillin with clavulanic acid
for the period of 1–5 days before the surgery. It was shown
that 1-day prophylaxis is sufficient in preventing inflammatory
complications compared to the 5-day prophylaxis in all types of
fractures.15 Similar observations were made by Andreasen et al.16
in Denmark, who have shown that a single dose or 1-day
administration of antibiotic is sufficient to prevent infection in the
surgical treatment of mandibular fractures and that it performed
better than a 7-day therapy. This is a very important proof for the
lack of necessity to prolong treatment with antibiotics, and thus to
culture resistant strains. On the other hand, Miles et al.17 in the
United States have not observed any statistically significant
difference in a group of 181 patients treated surgically for
mandibular fractures, irrespective of the fact whether they were
given antibiotic postoperatively or not. The observations from our
clinic allow us to avoid antibiotic therapy in the patients with
fresh, uncomplicated and closed fractures of the facial skeleton.
Antibiotics differ significantly, as far as their prices are
concerned. Heit et al.18 compared the costs of 1-day therapy with
cetiraxone and penicillin G that were used for the prophylaxis of
surgical treatment of mandibular fractures. They proved that
cetiraxone is more efficacious and ~$350 (1,400 PLN) less
expensive than penicillin G. The costs of 1 day’s therapy with
antibiotics or chemotherapeutic agents to which Gram-positive
bacteria had similar sensitivity (>80%) was calculated with the
drugs: trimethoprim/sulfamethoxazole, imipenem, ciprofloxacin
gentamycin. Ciprofloxacin was the least expensive antibiotic
with efficacy against Gram-positive bacteria of 80% and >89%
against Gram-negative bacteria (the cost of 1-day therapy is
~2 PLN). The most expensive antibiotic is imipenem (~300 PLN).
The most efficacious drug here is gentamycin, in which case the
daily cost of treatment is ~3 PLN. Gram-negative bacteria display
a similar sensitivity to imipenem, ciprofloxacin and gentamycin.
The cost for the treatment of methicillin-resistant Staphylococcus
aureus (MRSA) skin and soft tissue is the lowest for linezolid,
whereas the total cost of hospital treatment of such infections
with antibiotics is the lowest for vancomycin. Our studies confirm
these observations for infections caused by Str. mitis and Str. oralis,
where vancomycin was the most efficacious from the perspective
of pharmacoeconomics.8 The difference in the bacterial sensitivity
makes it a challenge to create pharmacoeconomical analysis that
could apply to other countries. Poveda Roda et al. by reviewing
the previous study references concluded that amoxicillin with
clavulanic acid, moxifloxacin and clindamycin are preferred for
bacterial infection of dental origin. However, for nondental origin
infections, it is recommended to use clindamycin and fluoroquinolones,
preferably moxifloxacin, in order to cover the spectrum including anaerobic bacteria. Given our results from the
past 2 years concerning the bacterial sensitivity to clindamycin
and amoxicillin+clavulanic acid, being 60.2% and 59.8%
respectively, this therapy will not be efficacious.19

The graph presents the costs of treatment of infection of Staphylococcus aureus with particular antibiotics.

DISCUSSION
Yuvaraj6 showed the domination of aerobic bacteria in a group of
88 patients with maxillofacial infections, where the most
frequently isolated bacteria were Streptococcus. These results are
similar to those obtained in our study. However, the researchers
obtained much higher percentage of penicillin sensitivity in their
study, equaling to 81%, in comparison to the 50.6% sensitivity in
the group examined in our study. According to Molander et al.,7
Enterococcus has been the most frequently isolated strain in 100
cases of root-filled teeth with apical periodontitis. The researchers
have showed very small proportions of obligate anaerobic
Gram-negative isolates. This was also presented in our study.

Similar results were obtained by Ru et al.,8 who have also shown
that the most frequently isolated bacteria were the Streptococcus
strain. S. epidermidis was detected in 19% patients. This strain is a
commensal bacterium colonising skin and mucous. It might also
de be due to swab contamination; however, S. epidermidis produces
many virulence factors and forms biofilm, and was isolated in
sinusitis and is now considered as one of the major source of
nosocomial infections.9–12 Furthermore, S. epidermidis are the
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surgical treatment of mandibular fractures and that it performed
better than a 7-day therapy. This is a very important proof for the
lack of necessity to prolong treatment with antibiotics, and thus to
culture resistant strains. On the other hand, Miles et al.17 in the
United States have not observed any statistically significant
difference in a group of 181 patients treated surgically for
Kuriyama et al.\(^{20}\) have observed lower bacterial resistance to penicillin (38%), as compared to the 49.4% being the result of our study. However, they did not find any statistical differences in the therapeutic effect on using various antibiotics in alveolar osteitis post extraction.

In the past 2 years, *Streptococcus* was the most frequently isolated bacterial strain.

The antibiotics that are the most efficacious against *Str. mitis* and *Str. oralis* are penicillin and ampicillin. From the point of view of pharmacoconomics, gentamycin is the most advantageous antibacterial agent, effective against *S. epidermidis*, whereas vancomycin turns out to be the most efficacious against *Str. mitis* and *Str. oralis*. In the case of *S. aureus*, the best antibiotics are gentamycin and trimethoprim/sulfamethoxazole. The resistance results suggest that empirical therapy should be based on ciprofloxacin and gentamycin.

**COMPETING INTERESTS**

The authors declare no conflict of interest.

**DISCLAIMER**

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