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Contamination rate and economic evaluation for repeated use of medicated preservative-free unit-dose eye drops

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Abstract:

Introduction: Preservative-free eye drops are usually single-dose vials so that it is recommended to discard the vial upon first use even if there is any remaining solution. This study aims to discuss the infection possibility of multiple uses of these eye drops and evaluate the economic impact of such action. **Methods:** 80 vials were divided into 4 equal groups, with one control group (c) and three groups. Volunteers resembled three different installation techniques to simulate using these eye drops in reality. The vials were then recapped and kept in the refrigerator for 24 hours. Next, the remaining solution in each vial was cultured as well as group C vials, and contamination and infection rates were compared between each group against the control group. The infection probabilities were applied to a decision tree model to compare the cost of reusing the vials. **Results:** Group A results were (4/20) (20%) $P \geq 0.10$, while group B got only 1 out of 20 (5%) $P \geq 1.0$, finally group D (5/20) (25%) $P \leq 0.04$ and this was the only group that showed a significantly higher rate of infection (pathogenic rate) as an indicator to the importance of the instillation technique. The cost and savings ratio ranged from EGP 20.1 to EGP 20.4 for the base case according to the different instillation techniques. **Conclusion:** Reusing is associated with cost savings depending on the installation technique. Further real-world study is warranted as actual experienced patients expected to provide pragmatic conclusions.

2.2 Statistical Analysis

For the statistical analysis, 3 groups and 1 control group were tested for the presence of contamination in each group and calculate the percentage of commensal and opportunistic microbs. The frequency of each identified microorganisms in all the groups was done and stratified according to pathogenicity. Types of these microorganisms were also identified to evaluate if there was actually a significant difference between the 3 groups compared to the control group using fisher exact test. After identifying the microorganisms, the diseases it can cause was studied and the drugs that treat it were reviewed. The maximum outpatient treatment duration was recorded. The cost of the treatment was calculated by adding the cost of every product available divided by the number of products available which leads to the average cost per disease.MS Excel was used for recording and analysing the data and the alpha rate was set to be 0.05.

2.3 Economic evaluation

The decision tree was used to evaluate the consequences of deciding to reuse the eye-drops. The top level node was dedicated for the decision of reusing the remaining medication in the vial on a second day. Second, the branches which represented the available option or routes were filled according to the outcomes of groups A, B, and D and pathogenic rate recorded. Third, the leaf nodes which represent the outcome of each option were registered according to its cost multiplied by its probability.

For the sensitivity analysis, decision trees were held according to best case scenario and worst-case scenario. Best case being that all bacteria that are considered pathogenic and commensal not reaching the infectious stage (pathogenesis) following their low contamination percentage and only other bacterial that are pure pathogens are considered to cause bacterial infectious diseases like conjunctivitis, keratitis, and endophthalmitis which require antibiotic to treat the infected eye.

While, worst case being any foreign living organism can be infectious. The base case represents the normal opportunistic bacteria is being infective (pathogenic) and commensal bacteria is not infective (not pathogenic). It is well reported in the literature that CoNS bacteria have a low possibility of infecting normal immunocompetent people.[22] Therefore differentiation of CoNS types would have little impact on the provided care plan. All costs were calculated using EGP Oct. 2022.

Appendix:

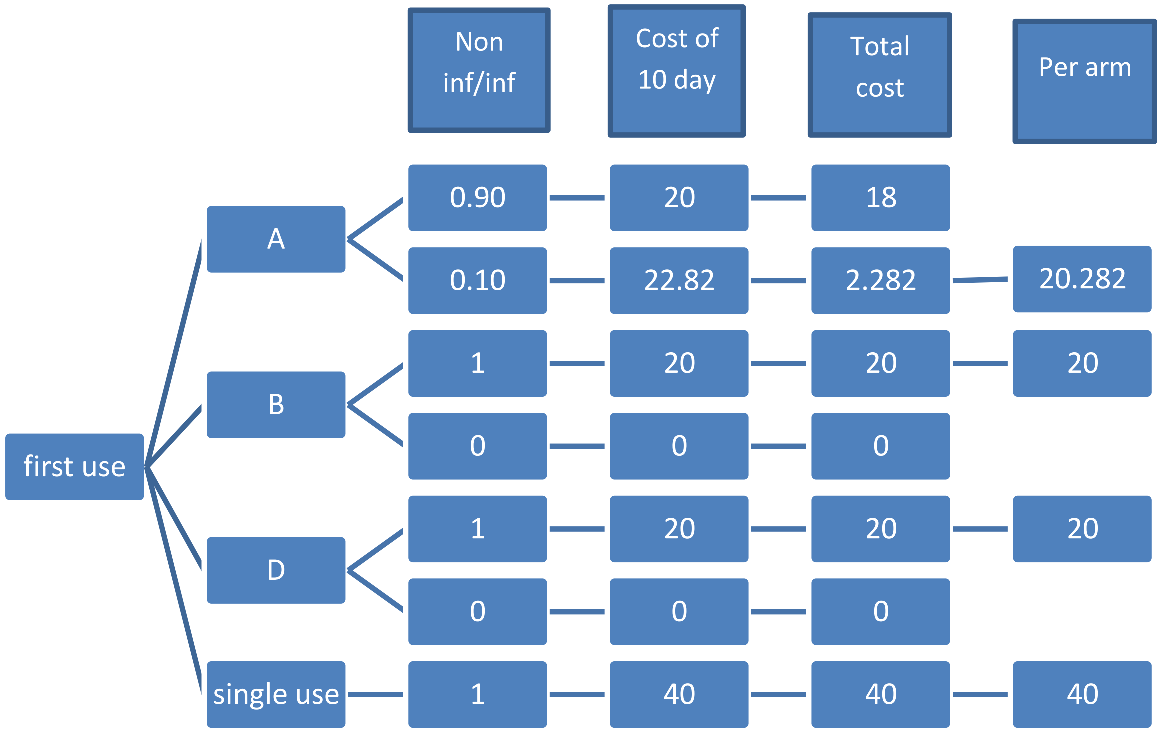
Appendix 1. disease caused by the contaminants of our study and its average treatment cost which is used to perform a decision tree.

S	Causative Agent[1,2]	Disease	Treatment	Treatment average cost
1	SA	Keratitis Conjuctivits Blephratis Prob: 0.05 rare	-Chloramephenicol tobramycin -fusidic acid	5.375 EGP 22.816 EGP 19.43 EGP
2	*Fungi*	Keratitis agriculture season Prob: 0.001 extremely rare worst case	Natamycin voriconazole	37.5 EGP 725.2 EGP
3	Gram-	*Keratitis pesdomonas arginosa* *Conjunctivitis e coli* *Prob: 0.01 very rare*	tobramycin	22.816 EGP

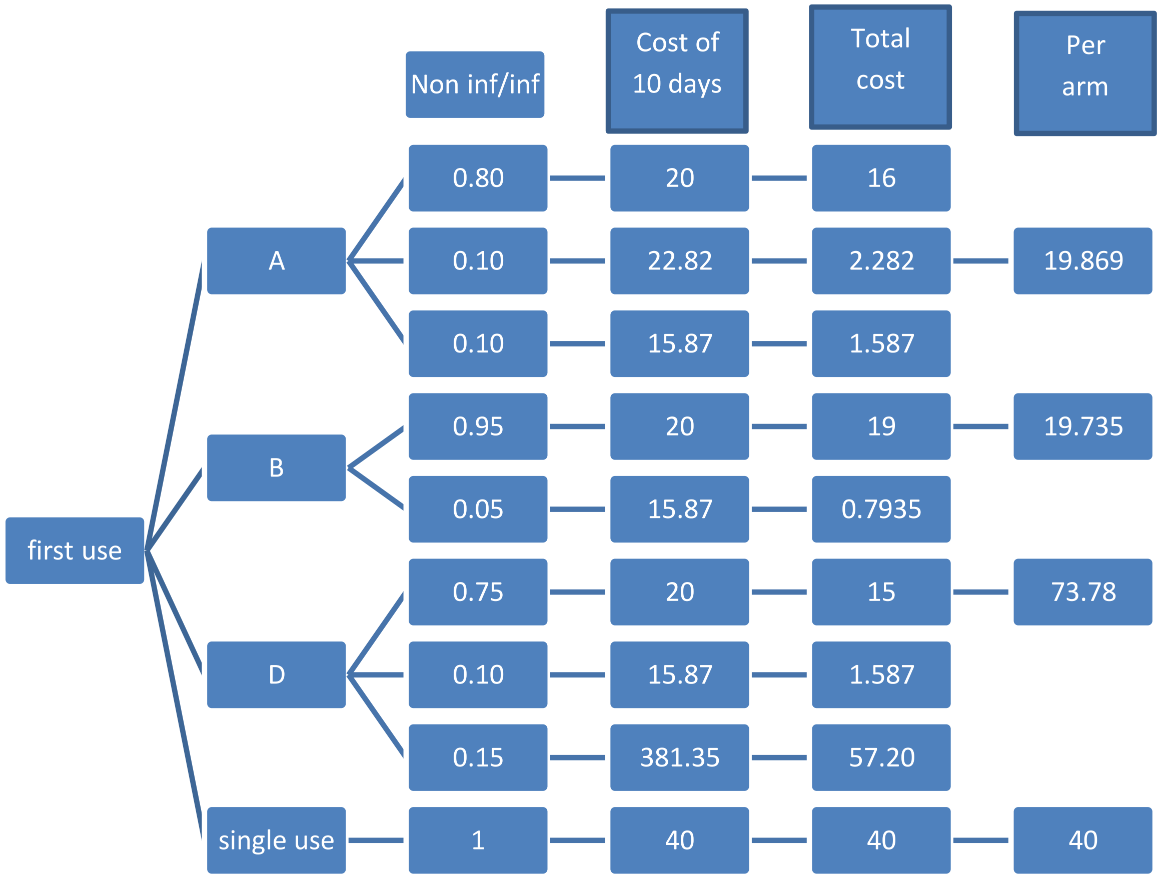
[1]Teweldemedhin, M., Gebreyesus, H., Atsbaha, A. H., Asgedom, S. W., and Saravanan, M. (2017). Bacterial profile of ocular infections: a systematic review. *BMC Ophthalmology*, *17*(1). https://doi.org/10.1186/s12886-017-0612-2
[2] Forrester, J. V., Dick, A. D., McMenamin, P. G., Roberts, F., and Pearlman, E. (2016). *The eye: Basic sciences in practice*. (4th ed.) Elsevier. https://doi.org/10.1016/C2012-0-07682-X

Appendix 2. **Conceptual Model for getting an eye infection:**

The patient reusing the vial is expected to take 2-3 days to develop symptoms of infection. Then take about one day for medical consultation that will refer them to topical treatment. After that, the duration of treating this simple infection is between 3-5 days Lastly, one day is needed for complete resolution.



Appendix 3. decision tree (best case)



Appendix 4. decision tree (worst case)