"Science without conscience is only ruin of the soul" said F. Rabelais. Therefore, what consciousness are we talking about ? That of the scientist alone, that of his peers, or even the collective consciousness of a society, of the whole of humanity? For a long time, science thought itself capable of inventing, evaluating and understanding the stakes of its discoveries by its protagonists alone, but it is clear that this vision no longer has any relevance today. We have entered a new era, that of post-modernity; it is characterized by a questioning of science and its basic axioms, but also, a doubt as to the ability of its actors to consider all the dimensions of their discipline, as well as their legitimacy to choose in the name of the community. The stakes of science and technology are unprecedented, these two disciplines are at the heart of our lives and our future. Thus, they must be thought of and questioned, that in view of their potential consequences. The technique, but also the science that gives it body must be the concern of all. It is thus that democratization, in the sense of a participation of the whole society in what it counts of diversity of opinions, opinions and considerations must be necessary. The social community that can benefit or suffer the effects of scientific production is the very one that must decide on the acceptance or rejection of this production.

At first, our research consisted in finding at the heart of writings, reports and circulating information, the elements able to legitimize and support our approach and our questions. In this sense, we have formulated two writings that have tried to update and bring together the relevant elements for our reflection. The first was to take stock and summarize the problem of antimicrobial resistance. Then, in a second writing, it is the bacteriophages / phagotherapy that have been the focus of a similar methodology. From these two axes: antimicrobial resistance, then bacteriophage / phagotherapy, we synthesized a third writing that aimed to show how our machine could meet the challenges of antimicrobial resistance through the use of bacteriophages. As a result, we had a machine that could respond to existing needs and problems, only as we explained with the history of science, we could not stop at that. Our project had to fit into the heart of society, not only in terms of theoretical issues, but also among the representations and requests of people who would have to be confronted with our machine, as patients or doctors.

In this sense, the Human Pratices symbolize and incarnate this much needed dialogue between science, its projects, its issues and civil and democratic society. This is why, within our project, its articulation and its development, it is essential for us to integrate this same democratic and informative approach. This is the very meaning of our different actions. These are not only passive approaches to registration of opinions, but a multitude of real consideration

of the fears, remarks and problems expressed, all of which will become part of the final development of the IGEM project.

1) Elaboration and intention of the survey

Regarding all the steps we have developed to integrate and cultivate Human Practice at the heart of our project, we will mainly focus the latter on the questionnaire we have developed and circulated to a wide audience. It gives us answers and remarks that are related to the other actions we have done. Note that in addition to this questionnaire, we interviewed two physicians specializing in infectious diseases, the interview of a patient who received phage, that of a doctor who had used the latter years before (before renewal of enthusiasm that the phages are now generating), and finally several interventions / presentations of our project during thematic weeks and other events related to science and intended to interact with society, the curious, the specialists and citizens of all ages.

The questionnaire had the advantage of probing and discovering that they could be the theoretical or practical "stop points" that could prove problematic in our project and in the final form of the machine. However, it is clear that to consider the possibility of acceptance or rejection of the machine that is our project, it was first necessary to know the state of acceptance, rejection or information of the public on the two main themes of our thinking: antimicrobial resistance and phages. Indeed, without prior knowledge in these two areas, it appears that it is especially necessary to provide information, while in the case of knowledge already effective, we must probe the latter and identify the problematic issues , oppositions, remarks, representations or public reluctance.

Prior to any use of our machine, it is the phages, the phagotherapy, as well as the antimicrobial resistance in what they represent and convey that we must identify in the society, without which, any step of information, of public discussion or education would be difficult.

Thus, our questionnaire was articulated around the following purposes: first, to identify the knowledge and the representations of the people questioned and consequently the absence or the presence of knowledge on the phages (which represent the heart of the project and the necessary for all its viability and acceptance). As a result, depending on the nature of this knowledge or the lack of it, seek to guide a personalized information and awareness campaign. Finally, it was to understand if there is a specificity of phagotherapy (representations, reluctance, fears or questions) to take into account for any use of this therapy; or on the contrary,

if phagotherapy is part of the same issues that are specific to the development and implementation of all new therapies.

From a methodological point of view, we proceeded according to the "funnel method" as presented in *Etude de Marché* by J. L. Giannelloni and E. Vernette.[1]

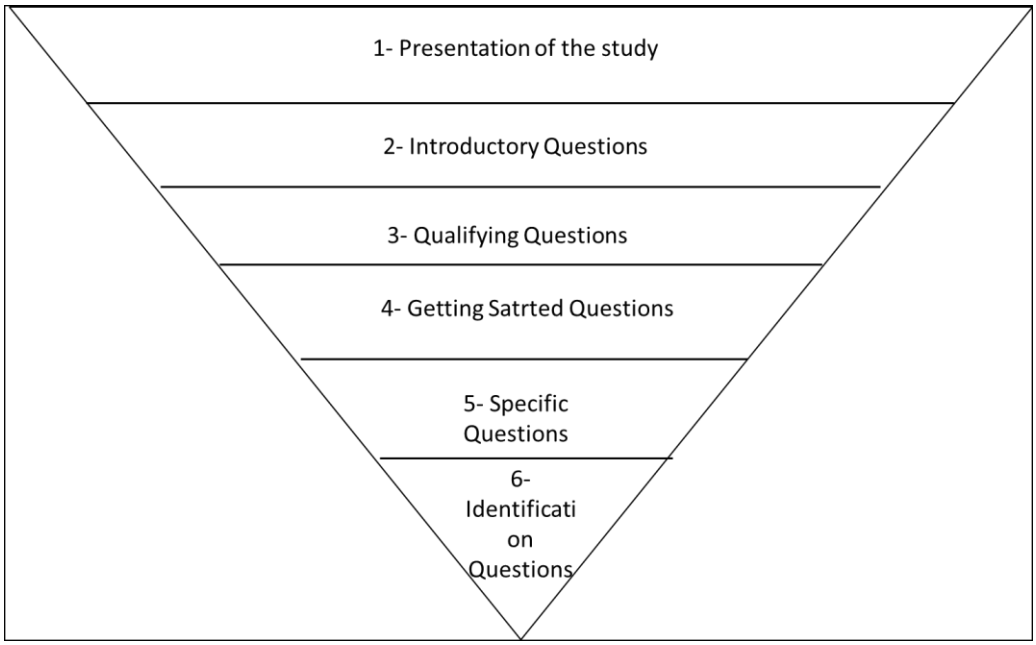


Figure 1. Funnel Method use for our survey

Thus, we started the questionnaire with a short presentation of the IGEM competition in general, as well as an explanation of our approach, without giving any elements likely to influence our sample group. Then, we wrote 3 questions to inform us of the degree of knowledge or true intuition that our sample group can have regarding phages (identification, number of "deaths" in a ranking of "the most lethal entities of our planet "and the place of phages in the ranking of the most numerous entities on Earth). As a result of these questions, people were not directly referred to other questions but rather to a didactic and educational part that provided an explanation and a correction to the questions asked. The stated purpose was not necessarily to obtain good answers but rather to make respondents feel that phages are exciting areas of knowledge and research and that they may relate to certain aspects of our lives. Then, we did the same with antimicrobial resistance, without forgetting to add a form of humor. In the funnel method this part was considered as introductory questions. We then finished this

[1] Using this figure thanks to the memory (in French) of : RANNOU, Marion, *Successfully capture the attention of respondents during an online survey*. Gestion et Management, 2015, p. 21. Quote GIANNELLONI, J.L, VERNETTE, E., Market Study, Paris, Vuibert, 3rd edition, 2012.

part with a question about the IGEM contest itself. Indeed, we sought to know if the sample group was aware of the IGEM competition, and if so, by what means.

After these questions, the questionnaire began to take on a dynamic and discriminating form. In fact, people were invited to answer a first closed question about their knowledge of antimicrobial resistance. Therefore, a negative response made them arrive on a terminal, teaching and explanatory part about antimicrobial resistance and bacteriophages. This was the first "qualifying question" of our questionnaire, another step in the methodological funnel. Moreover, at the end of the section on antimicrobial resistance and before the part on phages and phagotherapy, the discrimination is carried out again in order to obtain a sample group already informed and able to respond to our questions. These more specific questions then tightened the funnel of our methodology a little more. Finally, for all participants, the questionnaire ended with a question allowing their identification (age, profession).

In essence, our questionnaire was designed with a dual purpose: to inform and question. A didactic aim is the backbone, while those who are in a position to answer more specific questions are led to do so.

2) What about the results?

a. Our sample group

We have previously described our methodology, we must now focus on the results obtained. Overall, our questionnaire collected 338 entries. First, we must understand that the age of our participants (Figure 1) is mostly contained in the twenties (the youngest person: 15 years, the oldest: 69 years). Our sample group is young, which is probably inherent in the dissemination of our questionnaire (entourage, professional and social networks.) Nevertheless, this youth is not in opposition to a survey that is carried out for nearly a quarter in the health sector (doctor, health students, paramedical professions ...) ; a propensity that may be theoretically higher given the number of unspecified occupations (Figure 2). Our initial intention was not to question specialists on the subject, but rather to search within society in general to achieve the balance between information through the questionnaire, while collecting a number of questions. elements from individuals with prior knowledge of antimicrobial resistance and phages.

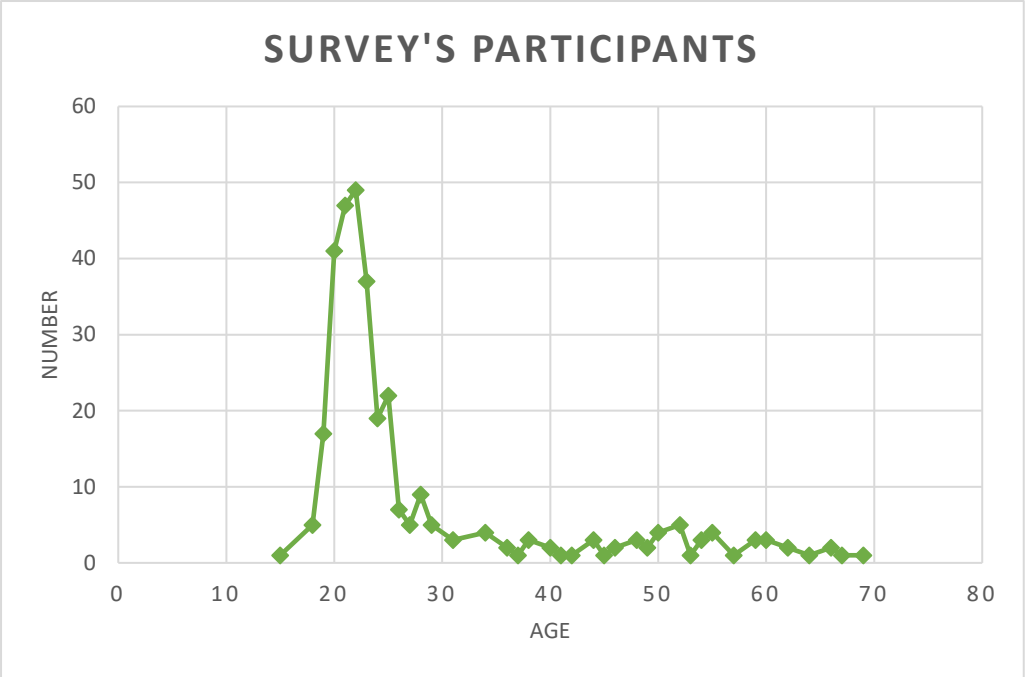


Figure 3. Curve showing the number of participants according to their age

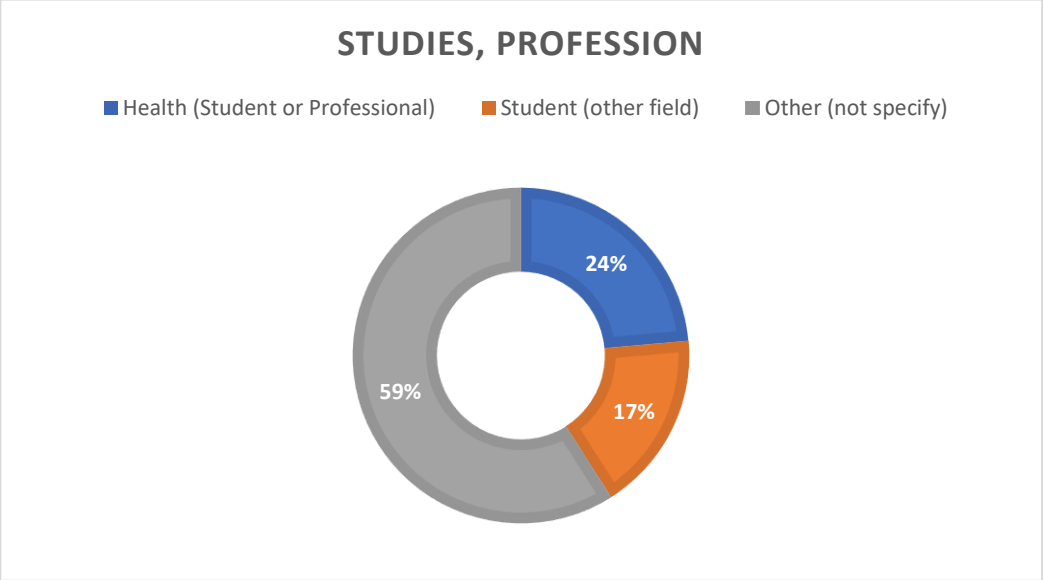


Figure 2 Professional distribution of our sample group

b. <u>IGEM Competition</u>

As for the IGEM competition, nearly 20% of our sample group does not know the competition, despite the short presentation at the beginning of the questionnaire. As for those who know it, it is for 38% of them, thanks to the medium of education (university, school) and for 23% thanks to the social networks. These figures tell us that the IGEM competition as such lacks a certain notoriety, it wins to be more known in the general population. The second

element to remember is the origin of this knowledge of the IGEM competition, here we can observe the role played by social networks and the school environment as vectors of communication. It is therefore the interest of IGEM projects to integrate a part of communication (social networks, forum, meeting and animations ...).

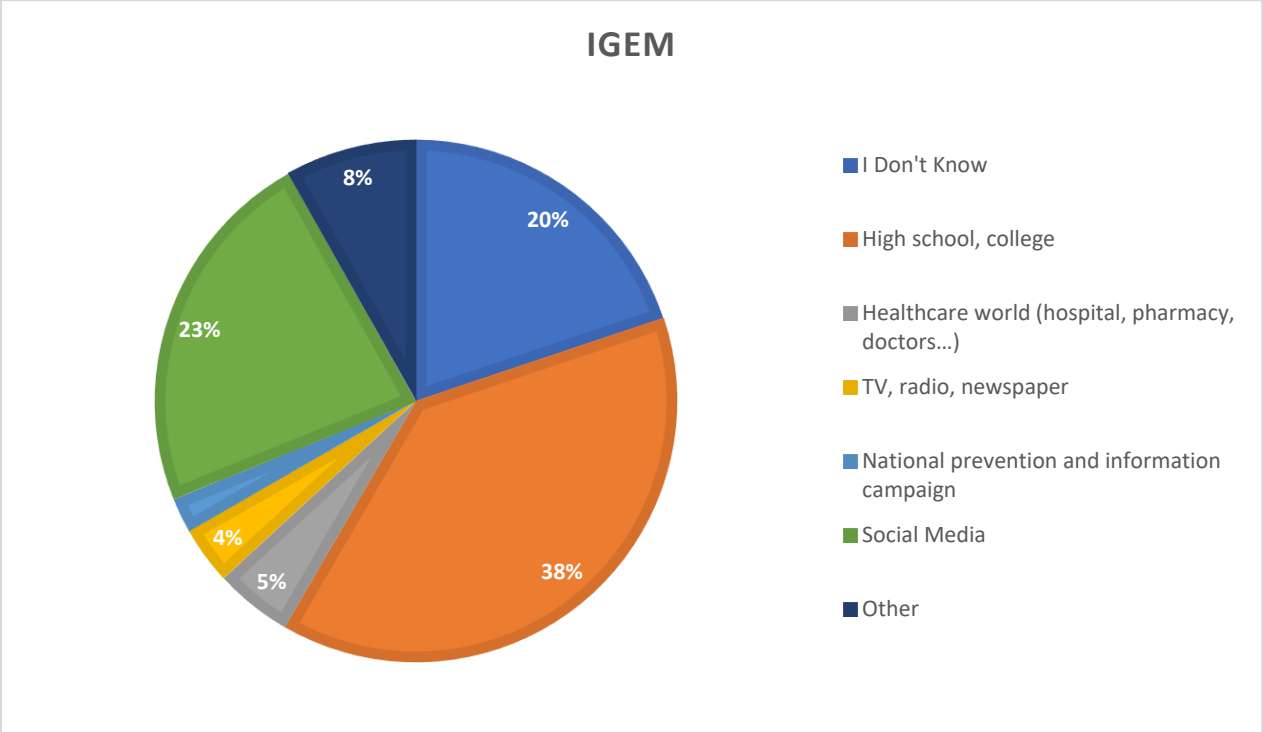


Figure 4. Proportion of the origin of knowledge of the IGEM Competition

c. <u>Knowledge test for informative and didactic purpose (figure 8 to 11)</u>

The role of this interrogative part was not to answer in an exclusively correct way, but rather to stimulate the curiosity of the sample group by facts setting the context of antimicrobial resistance, phages and phagotherapy. What we can learn from the analysis of this part is that the majority or at least the almost majority of the sample group has an intuition or a fair knowledge regarding antimicrobial resistance and phages. Nevertheless, there is always room for improvement to increase this proportion. We therefore believe that information campaigns, but also sensitization of the population are still useful actions, even necessary, especially if phages and antimicrobial resistance are, as we think, brought to take in the coming years a bigger place in the public debate.

d. Antibiotic resistance

Regarding our sample group, 80% of respondents believe that they know about antimicrobial resistance; an acquaintance whose origins are diverse. What we learn from this division is that the problem of antimicrobial resistance is encountered in different places and circumstances: education through school, by individuals when they are brought into contact with the environment as patients or caregivers, but also because of the media interest in this issue (reporting, dissemination of a national information campaign, etc.). We can still welcome the proportion of the reality of antimicrobial resistance given the proportion of caregivers who responded to our questionnaire. In addition, we must note that for more than 97% of our sample group, antimicrobial resistance represents a "major public health issue", just like the fight against AIDS, Alzheimer's or Cancer. This issue is also greater than or equal to a score of 7 (scale from 0 to 10) for 95% of respondents. A vision that is in line with the recommendations and findings of WHO.

Add, and this is an important point, that if 80% of our sample group is aware of what antimicrobial resistance is, this reality does not necessarily relate to the choices of everyday life. And for good reason, antimicrobial resistance is still largely linked to the medical world, which is why, if it is considered to be "very much" a factor in medical choices, this is not the case in the context of food or consumption choices. However, it should be remembered that the framework of agriculture and livestock farming is largely responsible, through the intensive use of antibiotics, of the explosion of antimicrobial resistance acquired. In addition, this antimicrobial resistance does not particularly affect human relations because it does not come into play at all in the relational choices with sick people.

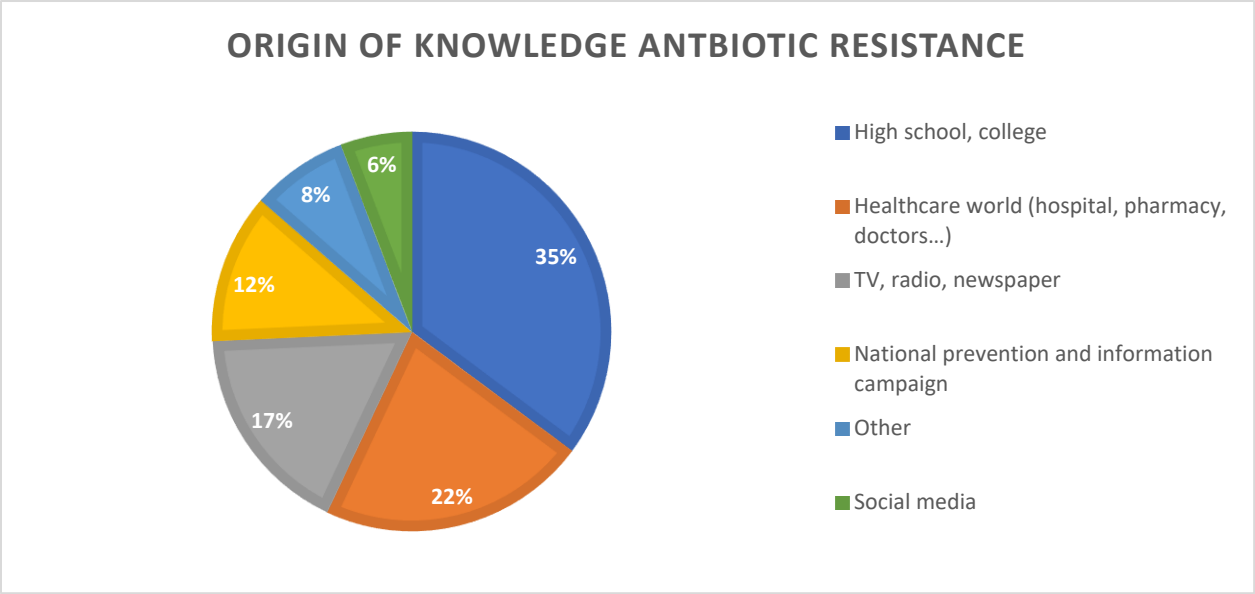


Figure 5. Origin of Knowledge Antibiotic Resistance

A final point that is important for us to underline is the representation of antibiotics as "trivial" or classical treatment. Indeed, we may suspect that intensive or immoderate use of antibiotics may be favored by misunderstanding of their efficacy and indication. In this sense, it is beneficial to know that 54% of the sample group has a "particular reluctance to use antibiotics". In addition, note that among this percentage, this reluctance is specific to antibiotics for 61% of respondents.

e. <u>Bacteriophages and phagotherapy</u>

Of the individuals who are aware of antibiotic resistance, 67% say they also know about bacteriophages and 17% do not know about phagotherapy. This leaves us to think that people can estimate knowing the bacteriophages without being informed of the therapy that uses them.

With regard to the origin of this knowledge, it is striking to note that for 54% of respondents, this knowledge comes from the school and teaching environment. Therefore, it does not seem absurd to say that the degree or nature of phage knowledge is related to the content of the studied pathway. Indeed, phages and their explanation is included in the curriculum of medicine or pharmacy. As a reminder, 24% of our sample group consists of students or individuals who have studied in a medical or paramedical field. Phage are not yet a topic particularly mentioned in the media, only 10% of respondents were informed of the existence of bacteriophages through the media. The general trend and this finding also prevails for phagotherapy.

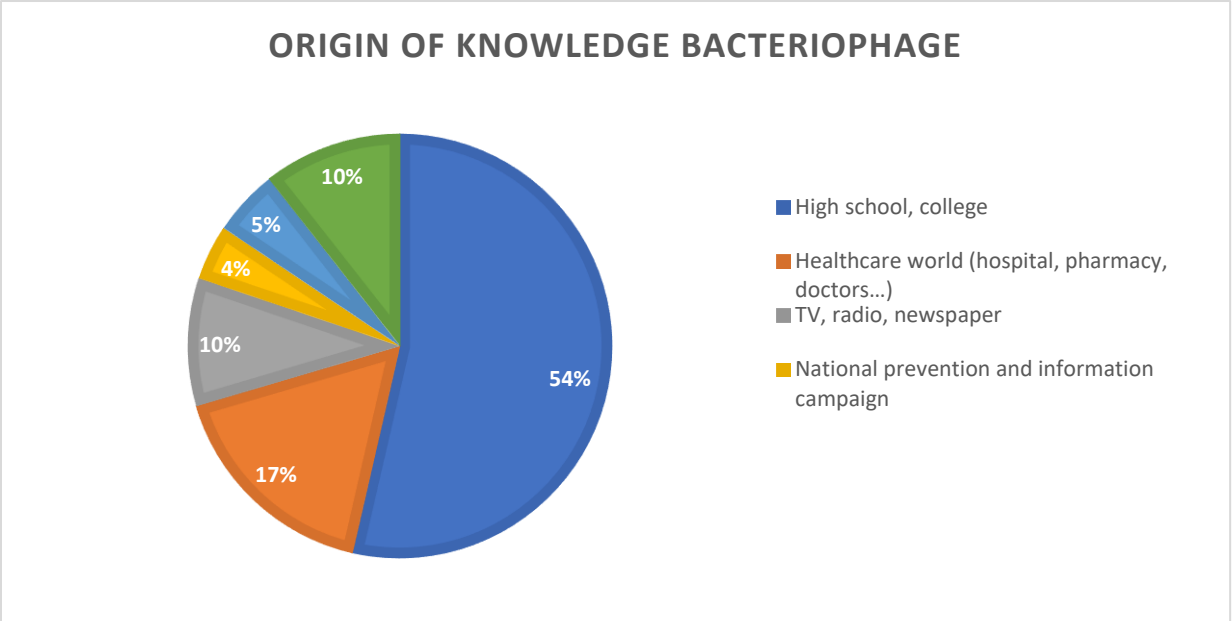


Figure 6. Origin of knowledge bacteriophage

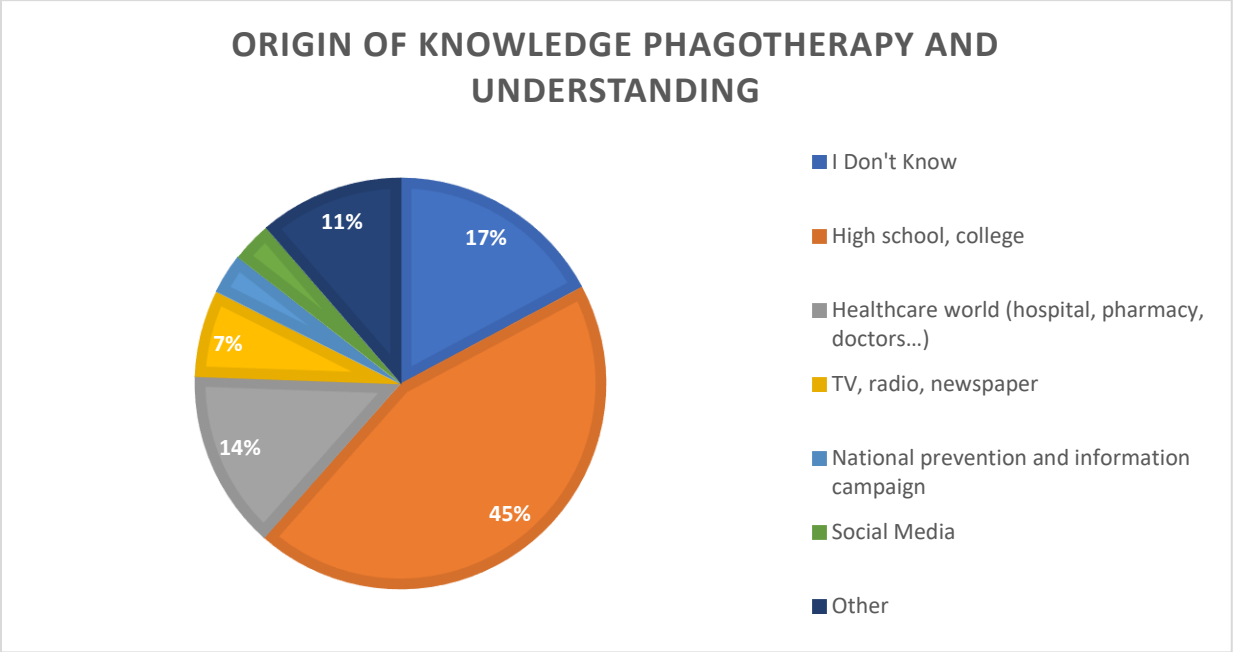


Figure 7. Origin of Knowledge Phagotherapy and Understanding

If we analyze in more detail the content of the responses concerning bacteriophages, we observe that in the state of their current knowledge on the subject, for 65% of respondents, phages can be a complementary therapy to antibiotics. The second strong trend is that of "I do not know" which accounts for 33% of responses. The categorical "no" is only represented in 2% of the answers. What this distribution tells us is that people are generally confident in the usefulness and feasibility of phagotherapy. Nevertheless, we must not ignore that more than a third of respondents do not know how to pronounce on this question. This trend is also observed

when we ask people about the possibility of using phage therapy. We get a large share of yes (59%) and a significant share of "I do not know" (36%). In case of treatment, for a large majority of individuals (61%), expectations and feelings about this therapy would be the same as for conventional antibiotic therapy. It should nevertheless be noted that for some of the respondents who have justified their choice, the experimental nature and the representation of this treatment as "innovative" increases the expectations for efficiency, but also the reluctance. This characteristic makes individuals wary while cultivating a form of hope and "last chance" in the face of a situation that could be a dead end without this therapy.

We can hypothesize that the form of indecision shared by some of our sample group is actually a lack of information on the issue. In this sense, when we inform or remind individuals of the harmless nature of phages, as well as their specificity, over 95% of them believe that these elements promote the acceptance of phagotherapy. In addition, when we inform individuals of the potential origin of phages (sewers, excrements ...), and remember the guarantee that they will be purified and therefore safe, this fact that could potentially be adverse to phagotherapy then has no impact on the confidence of respondents to the phagotherapy.

When we ask people to justify their choice, whatever it may be, the global trend informs us that what most people do not want to decide is the security and guarantee of the feasibility of phagotherapy. Moreover, it is the virulence combined with the specificity of the phages which is the most used element to the justification of its adhesion ; these remarks are all part of a conjuncture felt like that of the urgency to find solutions to antibiotic resistance. On the other hand, we must note that the precaution taken by the people questioned can be influenced by the "living" nature of the bacteriophages, because indeed, for 59% of them, the therapeutic use "of living organisms "(such as viruses), compared to chemical molecules represents a risk. This risk is for those who responded positively, inherent in the evolutionary and relatively autonomous nature of these organizations.

Note also that we speak of "living organisms" in quotation marks, we are aware of the particular aspect of viruses, which are not stricto sensu "alive". This choice of vocabulary is explained by the fact that we sought to evaluate the strength of certain representations, and not to correct or eliminate them. As a reminder, this questionnaire was intended to address the widest possible audience, this expression is used in this sense.

In addition, it should be noted that phagotherapy can be antibiotic therapy in the sense that it aims to eliminate bacteria, only it seemed to us that in the representations of the interviewees, as well as for the sake of clarity, we had to split antibiotics on one side and phagotherapy on the other. Indeed, several remarks made it clear that phagotherapy was literally

an antibiotic therapy. Indeed, an antibiotic is defined as a substance, of natural or synthetic origin, used against infections caused by bacteria. In this, phages are a form of antibiotic therapy.

Finally, in the case of using phages as part of a diagnostic tool, like our machine, we see an almost unanimous agreement of 95.5% of respondents.

f. Is phagotherapy a particular form of treatment ?

In the case of the evaluation and prioritization of the elements to be taken into account for an "acceptable" phagotherapy, the results give us elements of useful interpretations. First, it is the element of "security" that undoubtedly appears as a priority. In this regard, requests for clarification or additional information have no other purpose than to be able to judge the safety of phagotherapy. Second, efficiency is an almost equivalent priority in terms of responses. We find in this duo the basis of any pharmacological approach that is to evaluate the balance of benefits (effectiveness) / risk (safety) to judge a treatment and its interest. In third place, we find the "side effects". Indeed, their evaluation, as well as their frequency and intensity, are elements that must be taken into account when evaluating a treatment.

Then, at almost equivalent numbers of choices, we see the concepts of cost and the duration of the treatment, elements that are necessary but appear less important. On the other hand, we can say that they are conceived in relation to the head triptych we have mentioned. Indeed, a cost and the duration of a treatment can be put into perspective with regard to a benefit obtained or expected.

Finally, the priority is considered to be lower as regards the mode of administration and the visual aspect, elements which, again, can be put into perspective with the threshold of the expected benefits and the effectiveness of the treatment.

In short, all these elements seem quite common to the classic pharmacological and medical problems. Nevertheless, for the sake of clarity, we sought to know whether this hierarchy and this order were, according to the interviewees, peculiar to phagotherapy. To this question, the result was quite clear, 80% of respondents answered in the negative. For them, phagotherapy is not part of a particularized and different form of taking into account the classic elements necessary for the development of a new therapy. The top trio represented by safety, efficacy and the avoidance of side effects is common to all therapeutic approaches. The guiding concepts guiding research on phagotherapy and phages therefore seem to be common to all

approaches to therapeutic innovation. In short, the paradigm of therapeutic research fits perfectly with phagotherapy in the context of acquired antimicrobial resistance.

In conclusion, our questionnaire made us understand the importance of information and involvement of society for the success of our project, and more generally for the success of phagotherapy. In addition, what appears in terms of phagotherapy / bacteriophage is the need for mass information on the subject, because of this may result in the acceptance or rejection of such therapy. Especially since our questionnaire tends to show that the reluctance of an individual is generally measured by the yardstick of his misunderstanding and ignorance. The information should not be kept strictly separate from the specialized curricula of certain school curricula, but rather be repackaged and shared within society. Indeed, our era is particularly marked by the non passivity of individuals in terms of health and therapeutics. Only for this to happen in the best conditions, it is necessary for society to find clear and accessible information, so is democracy and human progress.

Annex : Graphical visualization of the data

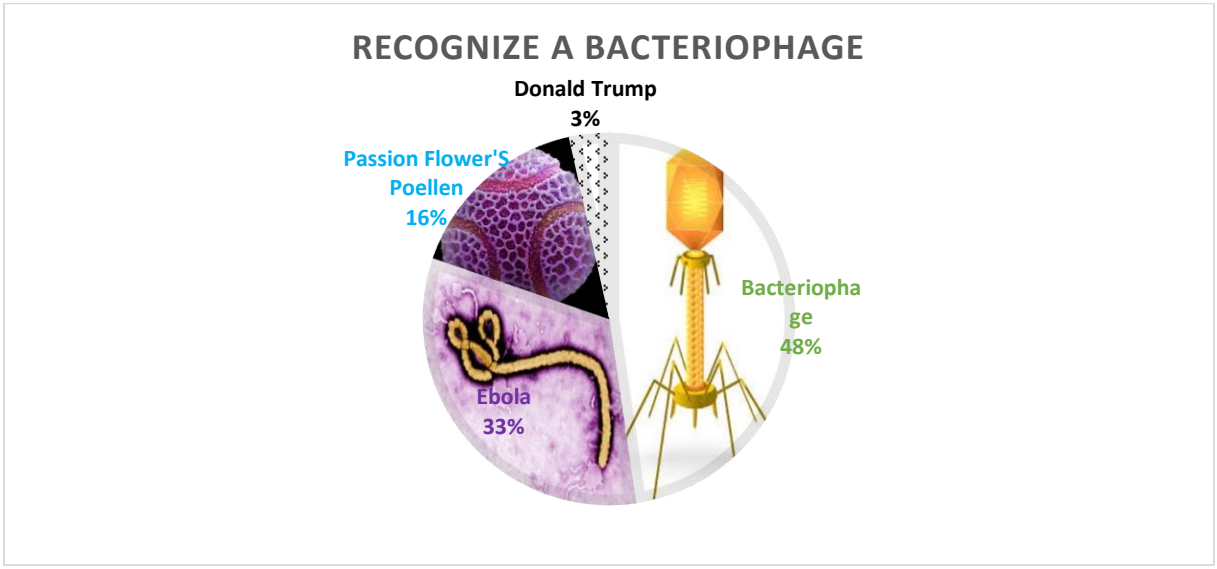


Figure 8.

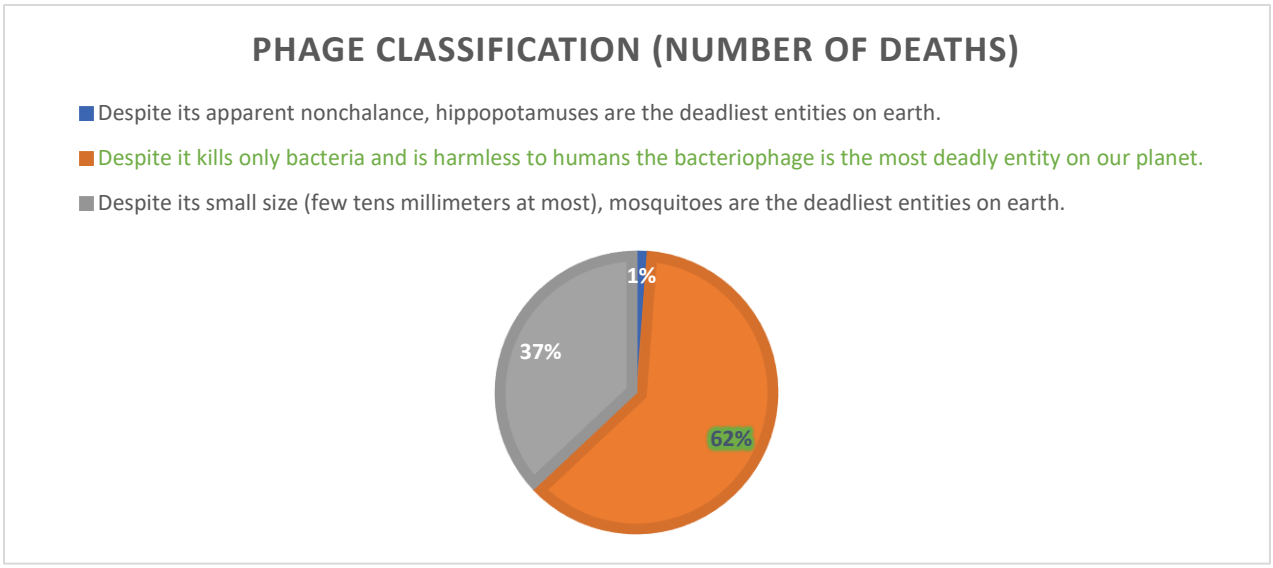


Figure 9

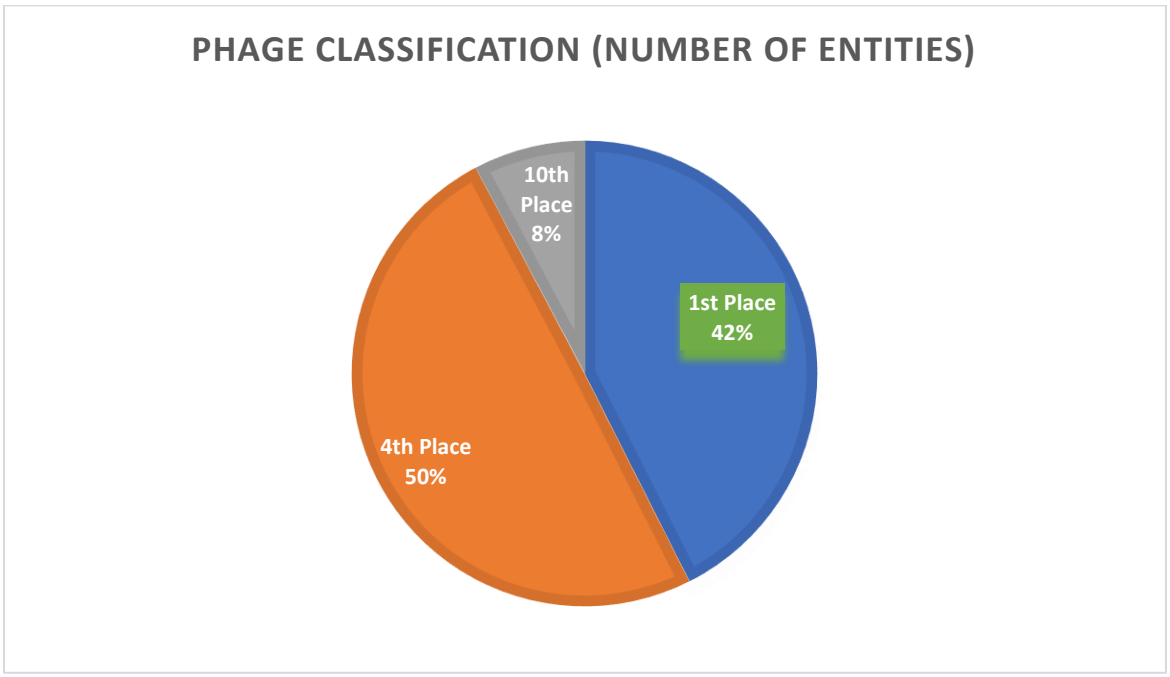


Figure 10

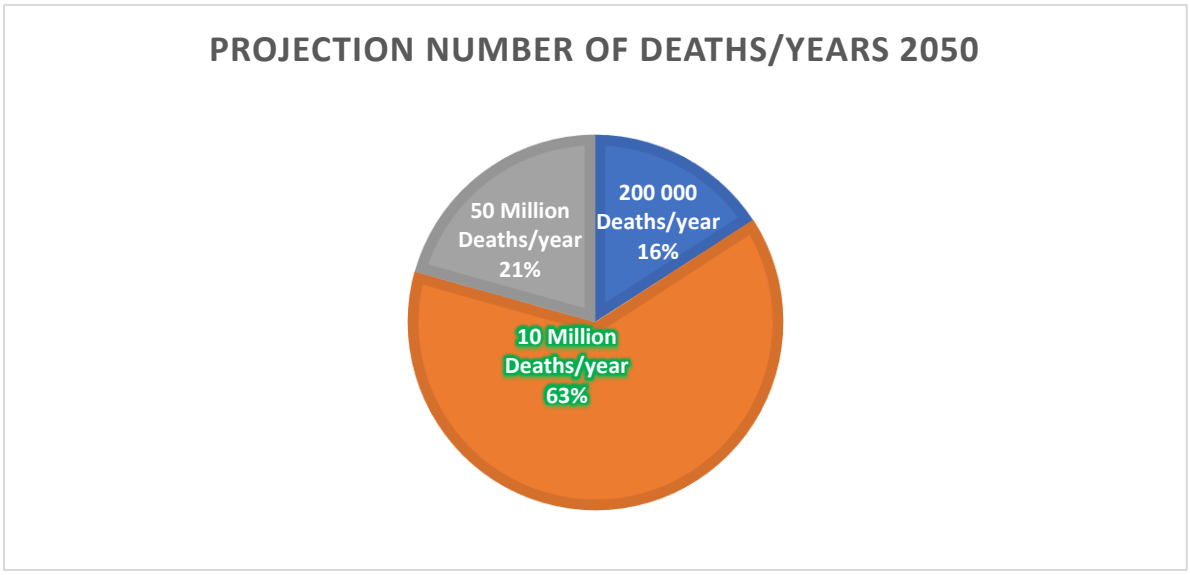


Figure 11

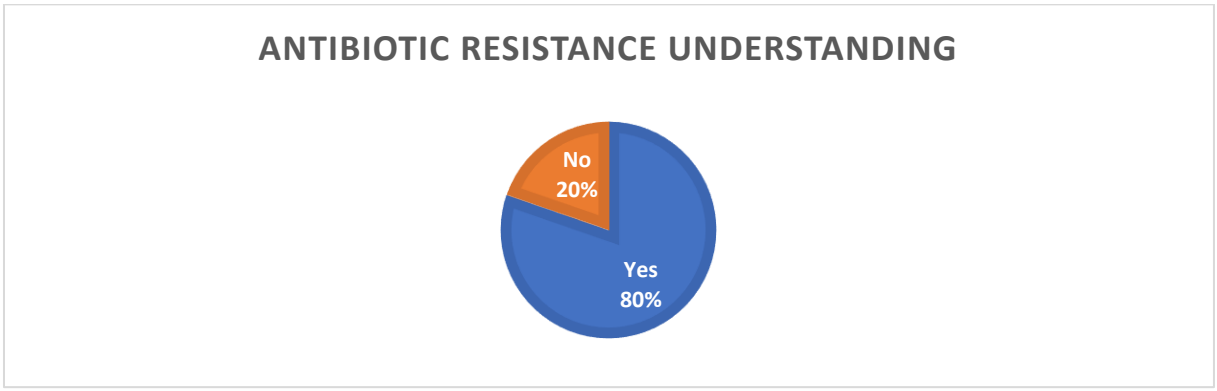


Figure 12

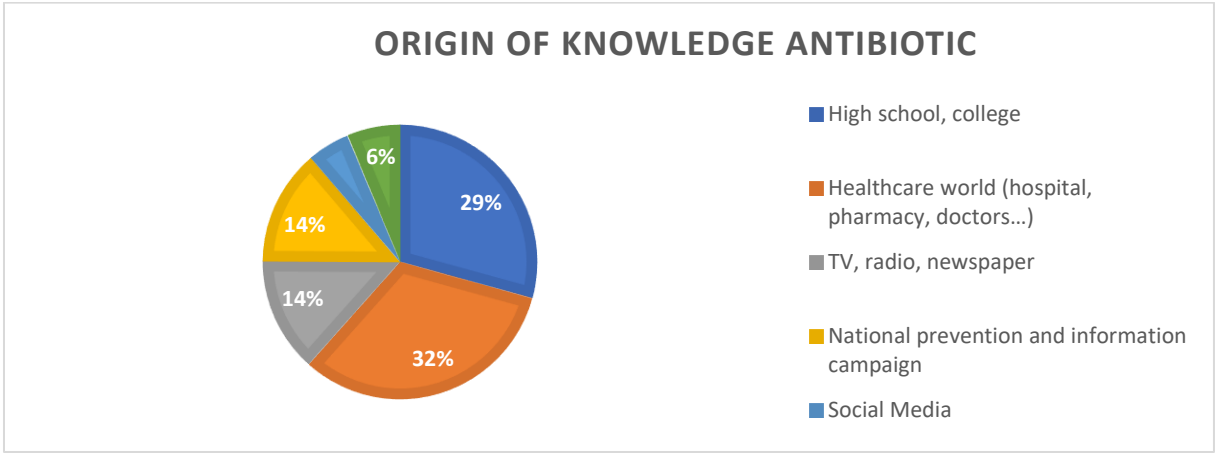


Figure 13

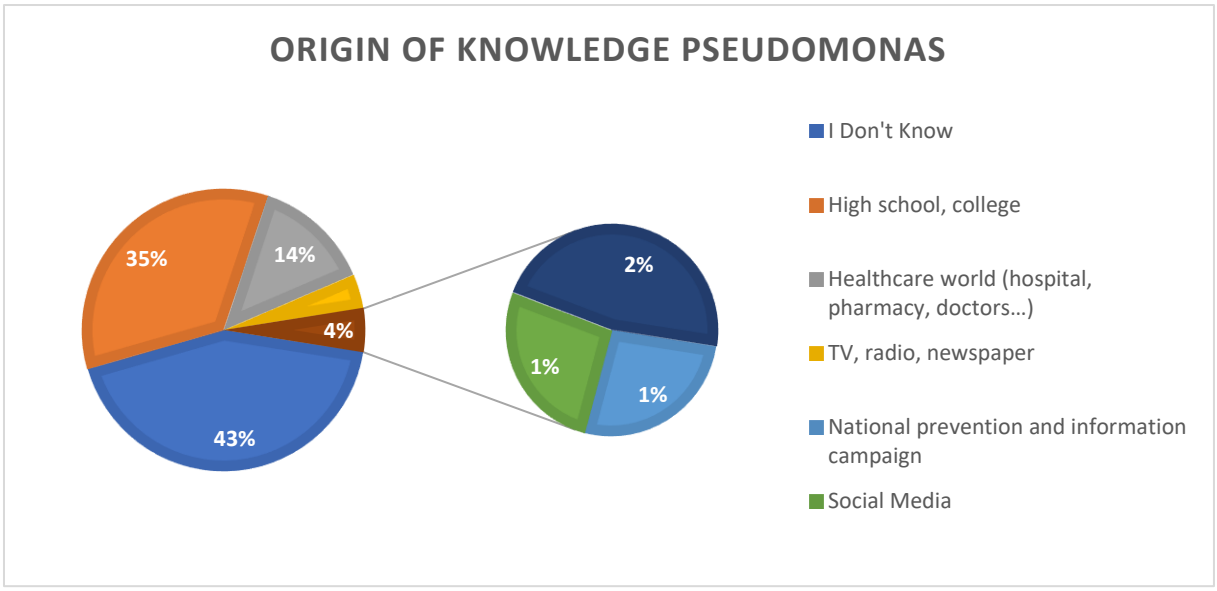
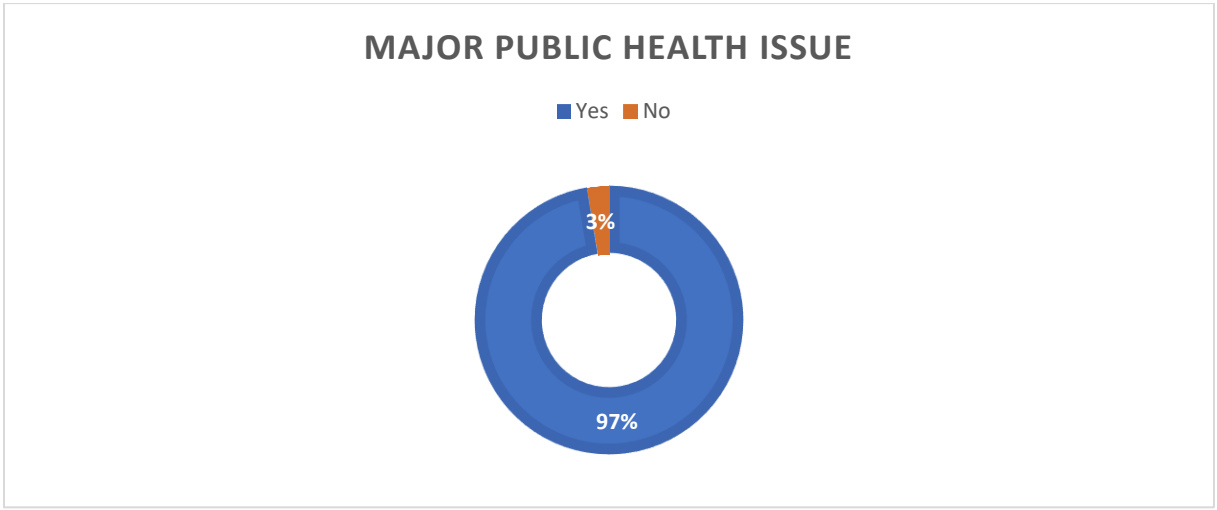


Figure 14



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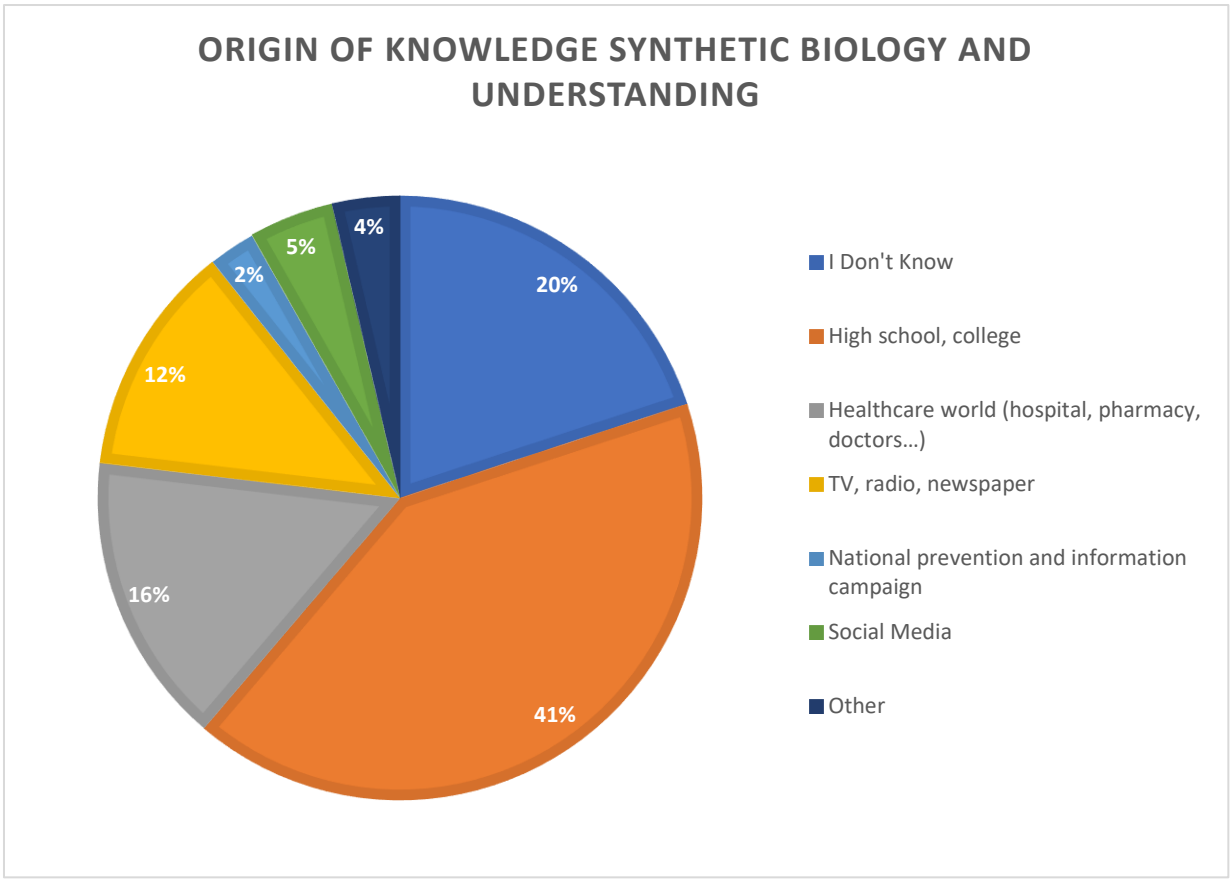

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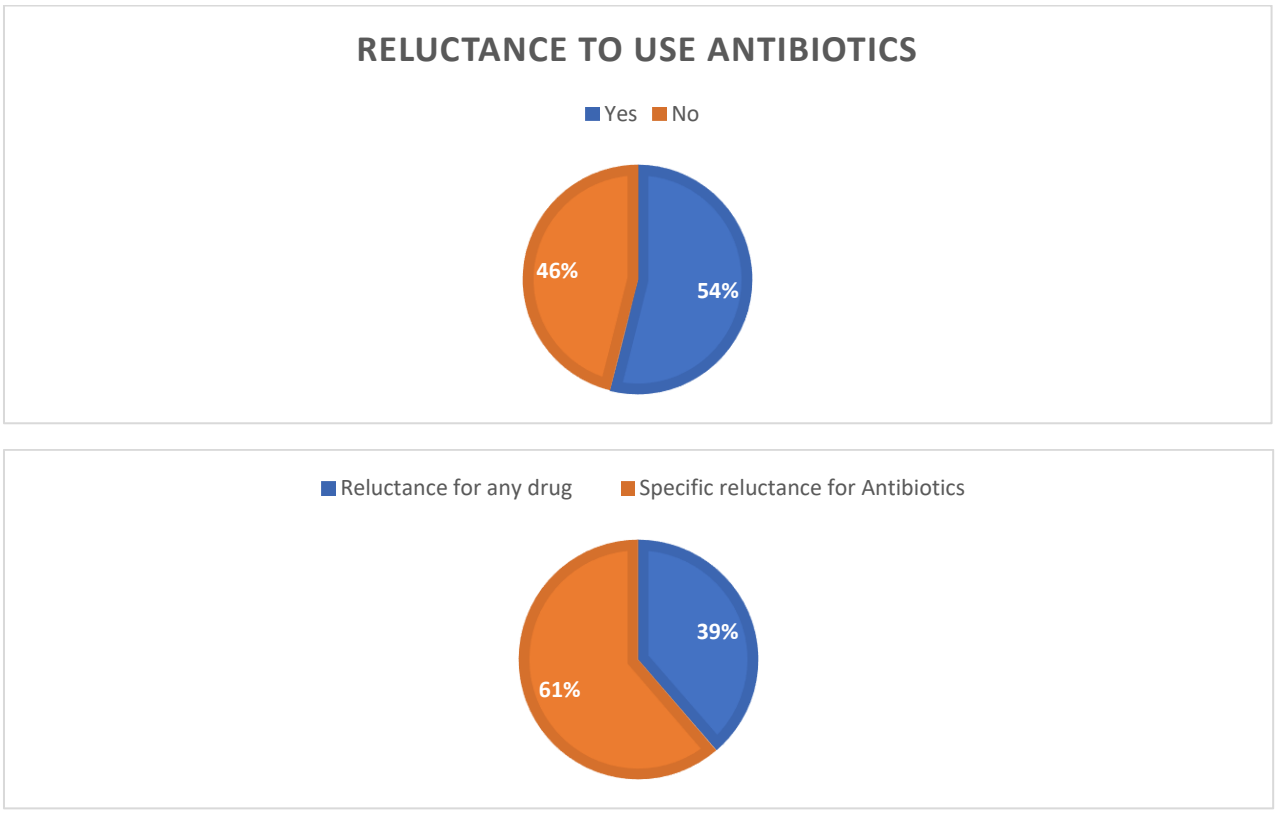
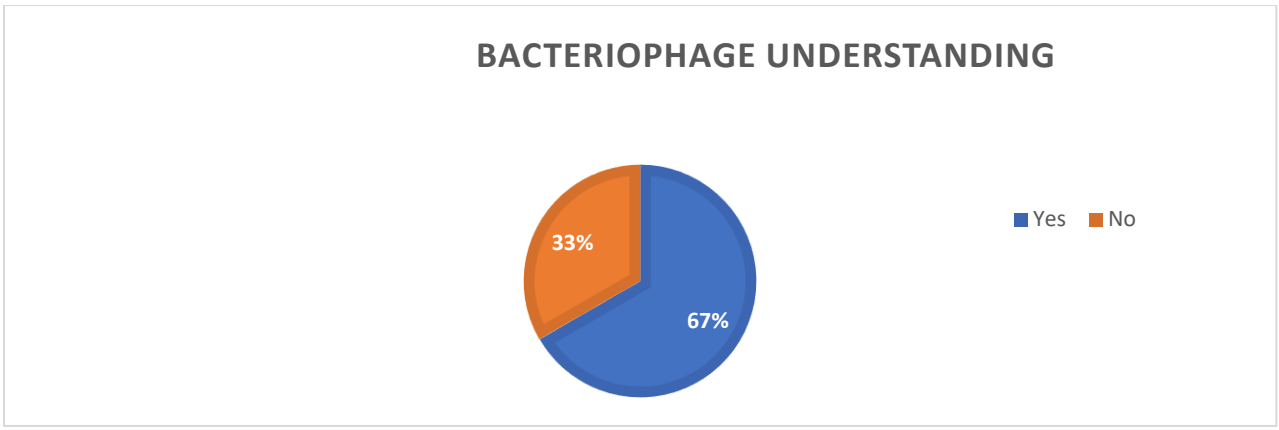


Figure 17. Reluctance for antibiotics and specificity



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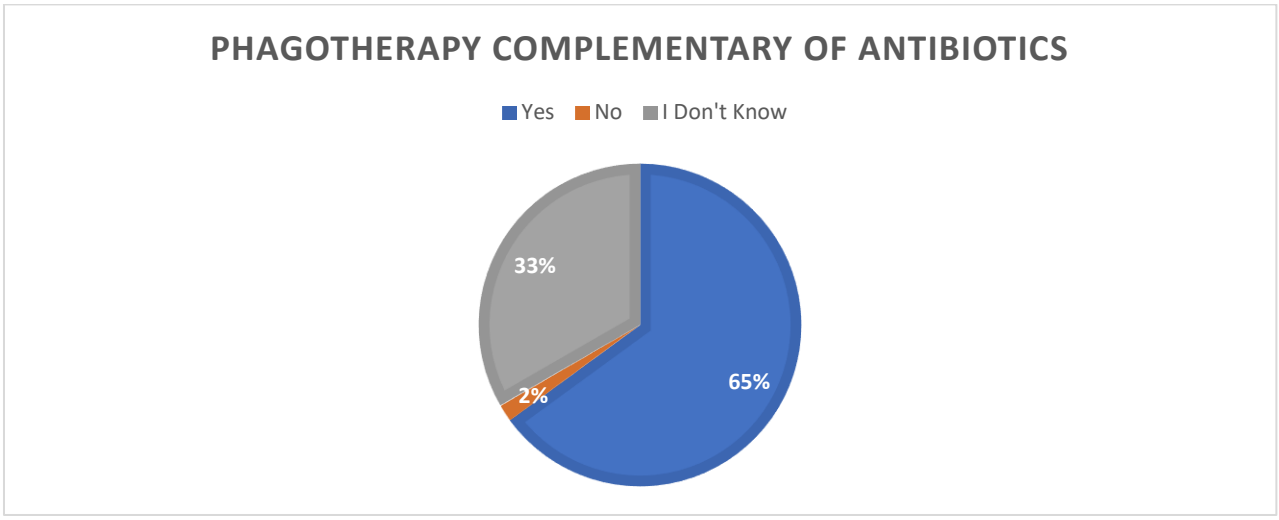

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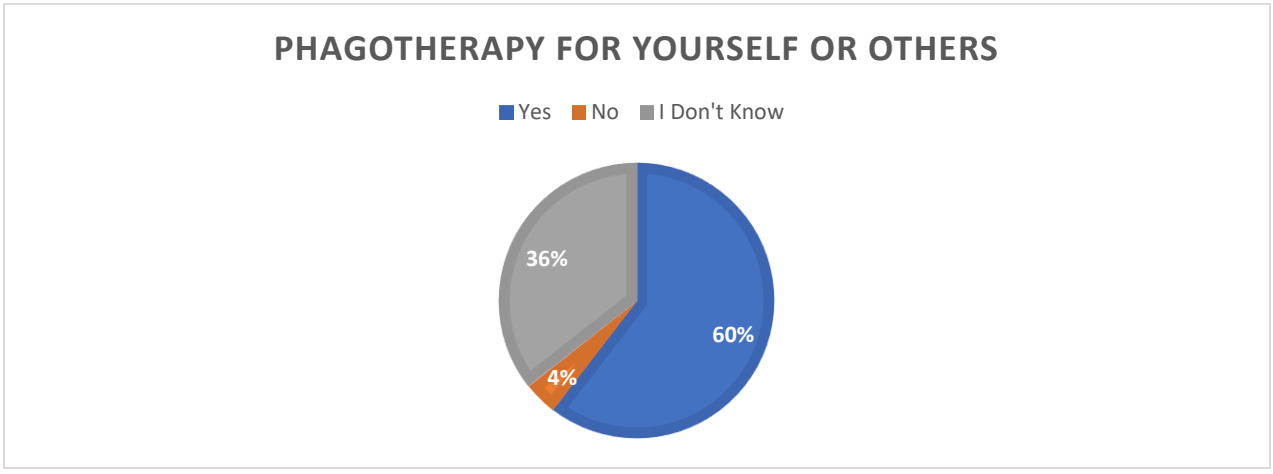

Figure 20

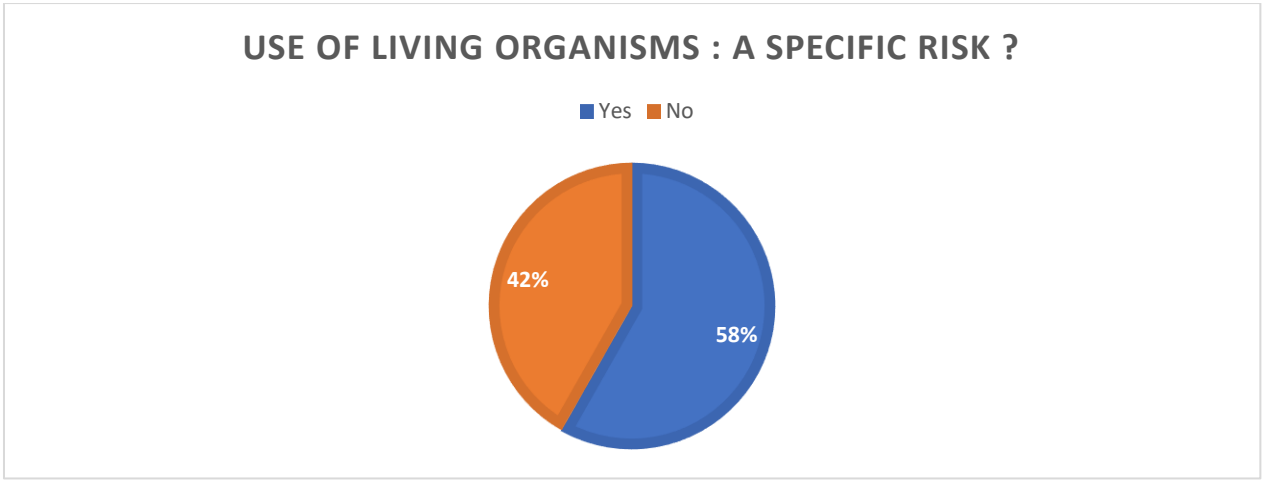

Figure 21

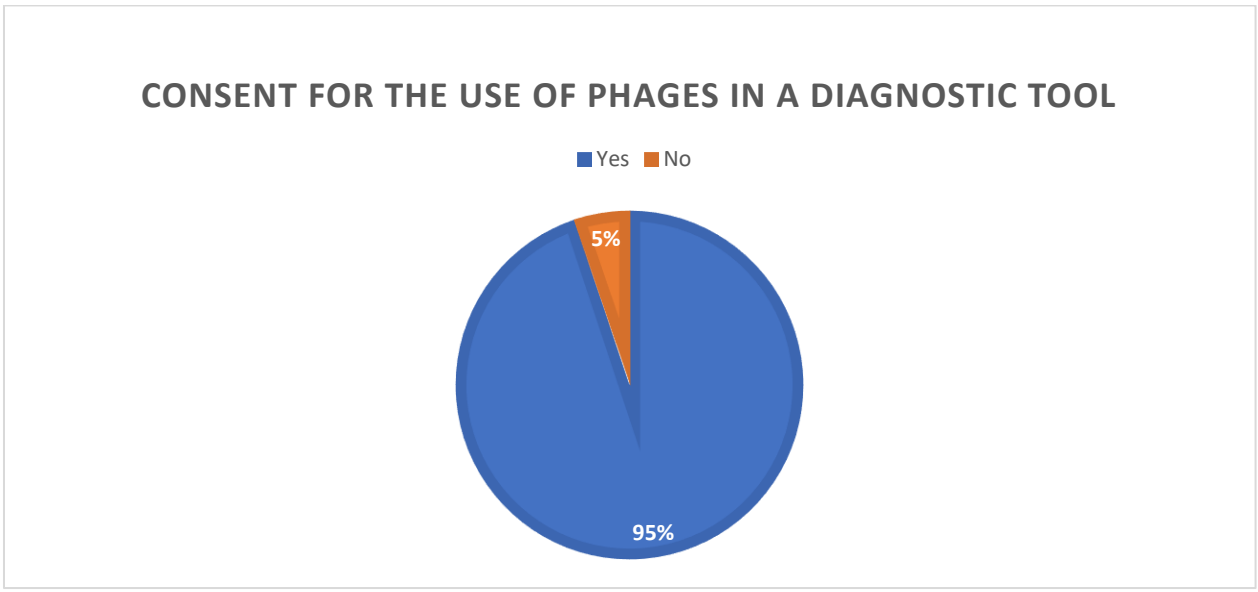

Figure 22