IJHSR
ijhighschoolresearch.org
REVIEW ARTICLE

# A Comparison of Production, Efficacy, and Safety of mRNA and Conventional Vaccines

Deniz Cenikli
Uskudar American Academy, Akasya Mah, Cecen Sok, Akasya Koru Sitesi, B3-C Girisi, Apt. No:46-G, Daire:183, Üsküdar/İstanbul, Turkey; dcenikli2005@gmail.com

ABSTRACT: This paper investigates the advantages and disadvantages of mRNA vaccines and conventional vaccines through a comparison of both, particularly in three areas: production, efficacy, and safety. Classical vaccines comprising of live-attenuated vaccines and inactivated vaccines. Live-attenuated vaccines use an attenuated version of the original pathogen whereas inactivated vaccines use inactivated germs. Messenger RNA vaccines, on the other hand, utilize mRNA containing the code for antigens. With this, the aim is to make cells build the antigens themselves. When these two are compared, it is seen that mRNA vaccines are faster to produce due to technological improvements. They are more effective than classical vaccines owing to the advancements in delivery systems. Moreover, they do not possess the risk of degradation of DNA or instability again due to technological development. On the other hand, inactivated vaccines are harder to produce because of developing cultures. They are not as effective as mRNA vaccines in SARS-CoV-2 and its mutations. Finally, live-attenuated vaccines have the probability of a reversion to the virulence of the natural germ. Thus, they cannot be given to people with weakened immunity. When all of these are considered, it has been concluded that mRNA vaccines have numerous advantages when compared to traditional vaccines.
KEYWORDS: conventional; inactivated; live-attenuated; mRNA; vaccines.

## Introduction

With the COVID-19 pandemic, all the attention of the scientists was drawn to a new type of vaccine: mRNA vaccines. This was a new approach to vaccination since conventional vaccines consisting of live-attenuated and inactivated (dead) vaccines have used entire pathogens that are either weakened (attenuated) or inactivated (killed) through physical and chemical processes for producing vaccines. However, the research on mRNA vaccines, in fact, dates back to the 1960s. During that period, mRNA vaccines had some deficiencies that needed to be improved. Owing to technological advancement in recent years, this was made possible for mRNA vaccines, especially for mRNA COVID-19 vaccines.

This research paper will investigate the general properties of conventional vaccines and mRNA vaccines as well as compare the two vaccine types with respect to their production methods, efficiency for preventing diseases, and biosafety that they possess by focusing on SARS-CoV-2. The paper starts with an introduction of the two types of vaccines mentioning their properties and some of their benefits and disadvantages. The conventional vaccine classification was made according to the information taken from the National Institute of Allergy and Infectious Diseases. The introduction continues with the comparison of the vaccine types in three main areas which are manufacturing, effectiveness, and safety including elaboration on some additional convenience and inconvenience of the vaccines. The paper is finished by showing mRNA vaccines have several advantages over conventional vaccines with respect to biosafety, efficacy, and production.

## Methods

***Conventional Vaccines:***

Conventional vaccines usually contain whole pathogens that are attenuated or inactivated so as to stimulate the immune system of the body against a pathogenic agent.[1] The first type of traditional vaccine is the live or attenuated vaccine. Attenuated vaccines are comprised of the weakened version of a virus or bacterium that causes the disease so that the germs replicate themselves several times and create an immune response in the body.[1] Most attenuated vaccines can create a strong and long-lasting immune response in the body against the disease with only one or two doses of the vaccine as the real pathogens and the pathogens utilized in this type of vaccine are very similar.[2] The virulence of these disease-causing viruses or bacteria is usually reduced by repeated culturing.[3] Since the pathogenic microorganism that is found in an attenuated vaccine is still a living organism even though it is weakened, live attenuated vaccines require refrigeration meaning that they need to be kept cool under low temperatures mostly between 2°C and 8°C (36 °F to 46 °F).[4] However, there are a few exceptions such as live varicella (chickenpox) vaccine which must be stored frozen within a temperature range of -50°C to -15°C (-58°F to 5°F) in a refrigerator.[4] Together the varicella (chickenpox) vaccine, measles, mumps, rubella (MMR) vaccine, shingles vaccine, and live attenuated influenza vaccine (LAIV) are some of the other examples of live vaccines.[5]

The second type of traditional vaccine is the inactivated or dead vaccine. In order to produce inactivated vaccines either



DOI: 10.36838/v4i4.5

entire pathogenic agents or microorganisms that are very similar to the germs are destroyed -or sometimes altered- through the agency of chemical agents, heat, or radiation after being grown in culture.[3] The aim of the destruction or alteration of the disease-causing microorganisms is to prohibit the replication of the replication of the disease-causing microorganisms.[6] A negative consequence of the destruction of germs is the decrease in the immunogenicity of inactivated viruses and bacteria provided by inactivated vaccines.[3] It is said that the immunity obtained from inactivated vaccines is generally shorter and weaker than the immunity provided by live attenuated vaccines.[3] Since the length and strength of the immune response of an inactivated vaccine are less, more doses of this kind of vaccine - generally two or three shots- are required to obtain a sufficient amount of antibodies in the body when compared to live-attenuated vaccines.[3] Although this may be a disadvantage of inactivated vaccines over live attenuated ones, an advantage of inactivated vaccines is the fact that the refrigeration process is not essential for some inactivated vaccines such as lyophilized vaccines in which the water is removed and they are vacuumed since the pathogenic microorganisms are inactivated through chemical or physical processes.[7] This eases the distribution of this type of vaccine around the globe as opposed to attenuated vaccines whose distribution is limited to the countries having refrigerators.[9] However, as usual, there are exceptions. Some of them are inactivated vaccines that are in a liquid state that do not contain aluminum adjuvants.[8] Additionally, inactivated influenza vaccine (IIV), hepatitis A vaccine, rabies vaccine, and polio vaccine can be given as other examples of inactivated vaccines that were developed until now.[9]

***Messenger RNA Vaccines:***

Messenger ribonucleic acid (mRNA) vaccines have been studied for decades dating back to the 1960s.[10] Recent advancements in technology in addition to the SARS-CoV-2 pandemic have extremely increased the speed of the development of mRNA vaccine technology. Messenger RNA is therefore a novel technology utilized to generate an immune response in the body.[1] Unlike classical vaccines, instead of entire pathogens, mRNA vaccines use mRNA in which the "blueprint" of a specific pathogen is encoded.[1] This allows the cells themselves to produce antigens (disease-causing proteins) which are normally found in the pathogenic bacteria or viruses by translating the information encoded in the mRNA.[1] Similar to live-attenuated vaccines, mRNA vaccines should be refrigerated. An exemplification of refrigeration can be given as the COVID-19 vaccine developed by Pfizer-BioNTech.[4] Since the durability and stability tests of the vaccine started quite late in the developmental process, refrigeration was imposed by the biotechnology company.[4] Likewise, another benefit of messenger RNA vaccines which is common to live-attenuated vaccines is their ability to generate strong immunogenicity, meaning that the body creates a strong immune response against the antigens that were produced by the body itself.[11] Yet, sometimes this immunogenicity might be exaggerated by the body causing the excess amount of cytokine which is a crucial and small protein used in cell signaling and produced by the innate immune system to appear in the body. However, there is no evidence supporting that "mRNA COVID-19 vaccines or even non-mRNA vaccines would result in cytokine storms".[12]

Two types of mRNA are currently being studied: non-replicating (conventional) and self-replicating (self-amplifying) mRNA.13 Non-replicating mRNA consists of a 5' cap structure that contains a 7-methylguanosine cap ($m^7G$ cap) that is connected to the first nucleotide by a triphosphate bridge, 5' untranslated region (UTR), immunogen information, 3' untranslated region (UTR), and a 3' poly-A tail respectively from left to right as shown in Figure 1 (a).[13] On the other hand, self-replicating mRNA, different from non-replicating mRNA contains an RNA-dependent RNA polymerase (RDRP) complex between 5' UTR and immunogen code which is an enzyme catalyzing the replication of RNA -in this case, mRNA- in addition to the components found in the structure of non-replicating mRNA as also shown in Figure 1 (b).[13] In other words, the RDRP complex that is located in the self-amplifying mRNA enables the mRNA to multiplicate intracellularly as shown in Figure 2.[13] The 5' $m^7G$ cap and 3' poly-A tail are used in both conventional and self-amplifying mRNAs to prevent the breakage of the immunogen blueprint by the enzymes found in the cytoplasm of the cells in the body.[13]

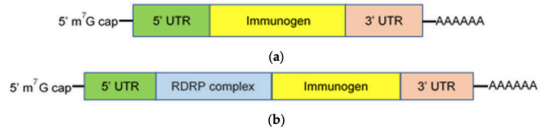


**Figure 1:** Non-replicating and self-replicating mRNA structures.[13]

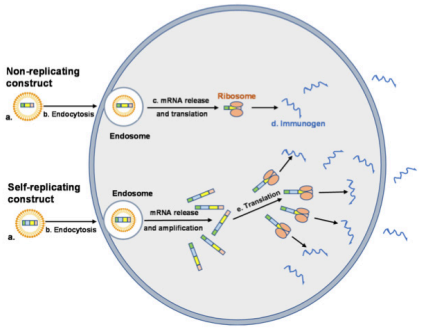


**Figure 2:** Production of immunogens via non-replicating and self-replicating mRNA.[13]

***Production of Traditional and mRNA Vaccines:***

Traditional vaccines take a longer time to be developed compared to messenger RNA vaccines.[1] In a nutshell, in order to produce live-attenuated vaccines first, wild bacteria or viruses are weakened under laboratory conditions.[3] The attenuation process might be done through heat or light although repeated culturing is the most preferred method.[3] Then, these viruses or bacteria are delivered to the body via live-attenuated vaccines. For inactivated vaccines, however, the methods such as using chemicals, radiation, or heat are used to destroy or kill the germs as can be seen in Figure 3.[14] After the inactivation, the destroyed pathogens are delivered to the body through inactivated vaccines Figure 3.[14]


DOI: 10.36838/v4i3.5

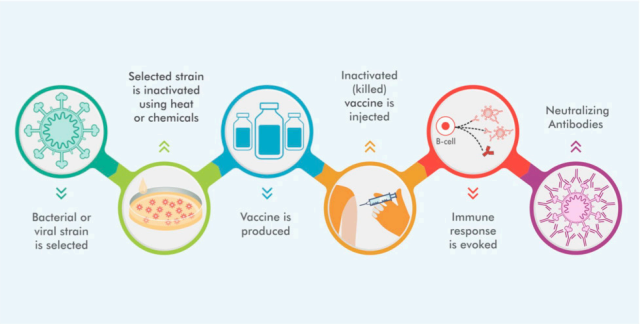


**Figure 3:** Production process of inactivated vaccines.[14]

Even though the description of the manufacturing processes of attenuated and inactivated vaccines seem to be short, indeed they are longer than the manufacture time of mRNA vaccines.[1] The average duration of vaccine development is measured to be 10 to 15 years.[15] One reason for this might be the fact that vaccine development comprises several stages: discovery and development, pre-clinical trials, human trials, licensing, manufacturing, and distribution.[16] To support this claim, the development times of several conventional vaccines from the discovery and development stage to the licensing stage (FDA approval stage) can be given. The vaccine for SARS-CoV-2 was developed in less than one year by breaking the fastest produced vaccine record.[17] In the meantime, the developmental time for the chickenpox (varicella) vaccine was 28 years, for the flu vaccine was 27 years, for polio was 13 years, and for mumps was 4 years.[16] Although the same vaccine development stages are applicable for mRNA vaccines as well, the time for the discovery and development stage is much shorter for them owing to the technological advancements in gene sequencing.[16] Specifically for COVID-19, the human trial stage was shortened as well as the discovery and development stage.[16] Another reason for the fact that traditional vaccines require a longer production time could be the culturing process in inactivated vaccines.[18] Since producing numerous inactivated bacteria and viruses takes up plenty of time, the discovery and development stage is longer for inactivated vaccines specifically, elongating the overall manufacture time for this type of classical vaccine.[18] Briefly, due to the differences in the manufacturing process, for the production of conventional vaccines, more time must be devoted.

***The Manufacture and Working Processes of mRNA Vaccines:***

Compared to traditional vaccines, mRNA vaccines have a different way of production and working as depicted in Figure 4.[19] First of all, the sequence of the pathogenic agent is identified via gene-sequencing.[1] Secondly, vaccines containing small and harmless mRNA fragments in which the code for the specific antigen -for COVID-19 this specific antigen is called spike protein- is encoded are produced and given to people.[1] Thirdly, mRNA fragments enter the body.[1] Thus, the body starts the antigen expression itself.[1] Simultaneously, the antigens are placed on the outer surface of the cells.[1] Finally, the immune system recognizes the foreign substance and starts to produce a suitable antibody for the specific antigen.[1] However, one disadvantage of using this process is that mRNA can be broken down readily.[20] Hence, it might be harder to produce enough antigens and subsequently enough antibodies to protect the body from the dreadful effects of pathogens. To reduce this disadvantage, two of the approved COVID-19 vaccines by Pfizer-BioNTech and Moderna are made utilizing self-replicating mRNAs so that the number of mRNAs is increased as was depicted in Figure 2.[13]

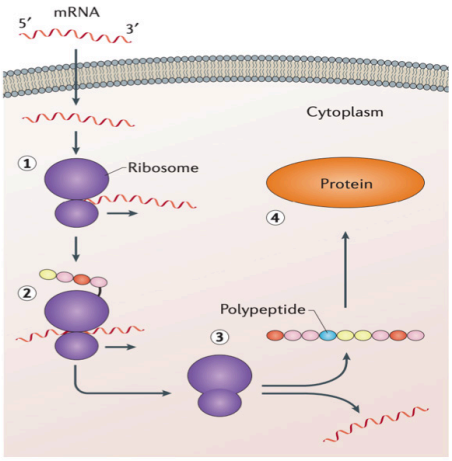


**Figure 4:** Working process of mRNA when it enters a cell.[19]

***Efficacy of Traditional and mRNA Vaccines:***

In the early usage of mRNA in research for vaccination, mostly naked mRNA was used.[21] This was creating several problems. The most important one was the instability of the mRNA which decreased the efficacy of the vaccines containing mRNA.[21] The mRNA was not able to reach the target cells safely because of the presence of nucleases which are the enzyme type that can break the mRNA down in the body.[21] Additionally, to reach the cytoplasm of the cell, mRNA needs to pass from a negatively charged phospholipid bilayer.[21] Only particles smaller than 1,000 Da (atomic mass unit) can pass through this bilayer.[21] Since mRNA is a much larger and heavier molecule, it required a carrier with it so that it could pass through the negatively charged bilayer.[21] Briefly, the deficiency of a well-prepared delivery system was the root of the problems.[21] However, this problem is no longer the case for mRNA vaccination due to the technological advancements in the mRNA delivery systems. There are several novel delivery systems divided into two big groups: viral and non-viral vector delivery systems.[18] Non-viral vector delivery systems can further be divided into two subgroups lipid and polymer delivery systems.[21] Some examples of lipid delivery systems are lipid nanoparticles and liposome complexes.[21] Some examples of polymer delivery systems are poly-amido-amine (PAA), poly-beta amino-esters (PBAEs), and polyethyleneimine (PEI).[21] Some examples of viral vector delivery systems are electroporation, polymer delivery system (polylysine), and cationic liposome.[21] Some examples of viral vector delivery systems are hybrid adenoviral vectors and retroviral vectors.[22] In this article, the main focus is on the non-viral lipid delivery system of lipid nanoparticles since the Pfizer-BioNTech, and Moderna vaccines both used this type

that mRNA can be broken down readily.[20] Hence, it might be harder to produce enough antigens and subsequently enough antibodies to protect the body from the dreadful effects of pathogens. To reduce this disadvantage, two of the approved COVID-19 vaccines by Pfizer-BioNTech and Moderna are made utilizing self-replicating mRNAs so that the number of mRNAs is increased as was depicted in Figure 2.[13]

In general, a rather popular method for solving optimization problems is Dynamic Programming (DP).[7] DP is essentially

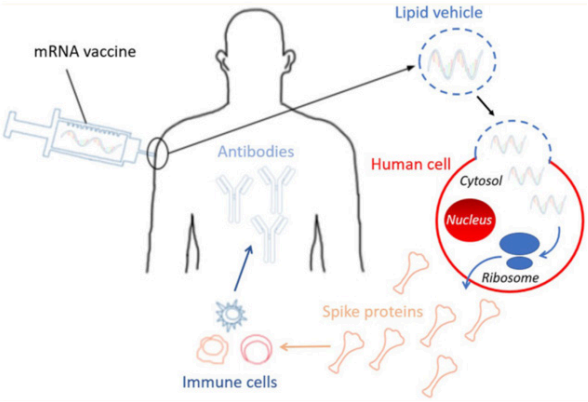


**Figure 5:** Fusion of lipid vehicle with the plasma membrane.[24]

a recursive solution with repeated method calls, storing the results of subproblems for the eventual solution. Compared to the aforementioned genetic algorithms, DP solutions usually use a lot of memory and have a longer running time. Even though genetic algorithms are typically harder to implement, efficiency in time and memory capacity are highly valuable assets for competitive programming which makes genetic algorithms more effective in Olympiad in Informatics.[8]

## Results and Discussion

Genetic Algorithms can be considered systematic random search algorithms where the random search algorithm also considers the optimality of previous trials and evolves accordingly. Randomly initializing the individuals causes the proposed solutions to span the search space. With each generation, the solutions then attempt to converge at a global optimum. Mutations add genetic diversity to the gene pool and aim to ensure that the point the population converges is the global optimum. Knowing these it can still be inferred that a genetic algorithm may not be able to converge on the most optimal solution even with the best possible parameters as it is still a randomized and probabilistic algorithm. Although that may be the case, it could be expected that the final result of a genetic algorithm is close to the global optimum. For the set of runs that will be conducted in this paper, it is assumed that the problem is solved if the value of the solution proposed by the algorithm is within 5% of the actual solution after 2000 generations. The percentage values of how close the solution is to the actual solution are calculated using the following formula:

Another factor to consider is that genetic algorithms are intrinsically parallel compared to most algorithms which are serial. Serial algorithms only permit linear exploration that does not store every value reached by the algorithm's “infer” steps. On the contrary, genetic algorithms contain multiple offspring which allows multiple dimensional explorations. Depending on the accuracy of the offspring, some are eliminated, whereas some are pursued as promising solutions. Due to the parallelism, they can operate resembling a graph structure, evaluating multiple traceries at once. Thanks to their structure, particularly problems containing vast amounts of potential solutions are easier to solve which would take an immense amount of time with a simple search algorithm.

***Identifying the sections of a problem:***

First and foremost, it is essential to identify crucial sections of a problem task before analyzing any algorithms or writing code. In this problem titled IPL, a certain number of games (N) are given according to the user's input. Afterward, N number of games is expected from the user with each containing a particular fee awarded if played in the game. The problem calls for the maximum amount of money that could be earned for an individual (Nikhil) through the N games. However, there is a condition in which an individual is obligated to play at most 2 consecutive games. Herewith, a certain algorithm must be constructed which maximizes salary while taking at most 2 consecutive game conditions into account.

Furthermore, a prediction about the complexity of a problem could be made per the given test data constraints. A maximum of $2*10^5$ number of games along with $10^4$ for each game can be inputted by the user. An average computer is able to make approximately $2*10^6$ calculations per second regardless of the operating system. Thus, a brute force algorithm with time complexity of $O(n^2)$ would be sufficient for a solution to pass this problem. The time complexity of $O(n^2)$ signifies the worst solution possible for a problem which usually persists in iterating through every single value until the correct answer is reached. Nonetheless, a brute force solution wouldn't pass for this problem if the user could input $2*10^8$ number of games. In a hypothetical case, a genetic algorithm would be one of the most ideal solution methods for this problem with

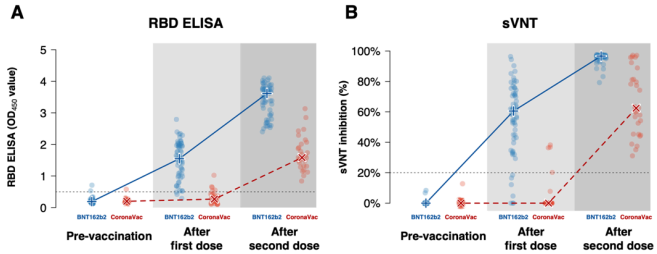


**Figure 6:** Comparison of BNT162b1 and CoronaVac vaccines antibody production and neutralization.[29]

the time complexity of O(gnm). Among the time complexity of O(gnm), "g" stands for the number of generations, "n" stands for the population size, whereas "m" signifies the size of individuals.[10] In brief, although in this particular case it's not imperative, a genetic algorithm solution would be a fast and viable solution to the problem among random search and brute force algorithms.

***Genetic Algorithms Implementation:***

The genetic algorithm is implemented via the programming language C# which is a general-purpose, object-oriented programming language developed by Microsoft. The following


DOI: 10.36838/v4i3.5

section breaks down the code into several sections - namely initialization, selection, crossover, mutation, and termination.

Before the function of the code is analyzed, its inner structure must be understood.[11] First of all, the code starts with a class named Individual, which represents one individual in the entirety of the population. Each contains a set of genes that are of template type, a double fitness value, and a chromosome length which is common throughout the entire population. Its implementation is as follows:

All of these instance variables are initialized with a constructor as each instance of the Individual class is created. Another structure within the algorithm is the Population class. The class contains an array of individuals, a generation number, a population size, a chromosome size, and various probability values for the genetic algorithm to work on. The implementation of its instance variables is as follows:

As evident from the code snippet, the population class also contains two functions: GetRandomGene() and CalculateFitness() functions. These functions are provided by the client of these classes and are called within the population's various functions. GetRandomGene() is the function that returns a random gene to initialize the members. CalculateFitness() is a function that returns a double value according to the genes of the individual; the number returned signifies the fitness of that particular gene set or individual. As cognizant of solely the meaning and implementation of these values, it is possityptype of delivery system in their SARS-CoV-2 vaccines.[23] This new lipid nanoparticle technology used by both of the approved and the most used COVID-19 vaccines not only allows the messenger ribonucleic acid to travel safely inside the body but also eases the entrance of the large and heavy mRNA molecule into the cell from a negatively charged phospholipid bilayer.[21] Whilst mRNA is entering the target cell, the encapsulating lipid fuses with the plasma membrane as described in Figure 5 by a model.[21]

Other than newly developed delivery systems, the effectiveness data of COVID-19 vaccines can be compared to show that the lipid nanoparticle delivery system has made the mRNA vaccines much more efficient than classical vaccines, specifically inactivated vaccines. In a study conducted at 99 centers in the United States where 96% of 30,420 volunteers received two doses of intramuscular mRNA-1273 injections 28 days apart, the efficacy of two doses of mRNA-1273 (Moderna) vaccine against symptomatic COVID-19 including severe diseases in persons 18 years old or older was found to be 94.1%, and no safety concerns were identified.[25] Yet, only transient local and systematic reactions were observed.[25] In the meantime, in the phase three trial of the BNT162b1 COVID-19 vaccine where 43,000 volunteers from roughly 150 clinical trial sites in several countries including the United States, Turkey, and Argentina, the overall efficacy of the vaccine was found to be 95% and the effectiveness of persons over 65 years old was recorded as 94%.[26] On the other hand, the efficiency data for the CoronaVac (Sinovac) vaccine which is a type of inactivated vaccine is lower than the ones found in mRNA vaccines when both are compared to each other. In a study in Indonesia where 1,620 healthy adults within an age range of 18 to 59 were injected with two doses of CoronaVac (Sinovac) inactivated vaccine 14 days apart, the effectiveness of the vaccine to prevent symptomatic COVID-19 was confirmed as 65.30%.[26] In a similar study conducted in Turkey, the same inactivated vaccine's efficacy against symptomatic COVID-19 was found to be 83.5%.[27] In another similar study conducted in Brazil where 43,774 people being 70 years old or more were given two shots of CoronaVac inactivated vaccine, the adjusted vaccine effectiveness against symptomatic COVID-19 was confirmed as 24.7% between days 0 and 13 meanwhile this value was found as 46.8% after the second dose.[28] In another study where the immunogenicity of mRNA vaccines and inactivated vaccines against COVID-19 based on BNT162b1 mRNA vaccine and CoronaVac inactivated vaccine were compared, the resulting graphs showed that both the amount of antibody produced by the body and the neutralization amount is higher in the BNT162b1 mRNA vaccine compared to CoronaVac inactivated vaccine as can be seen from the graph in Figure 6.[29] The relationship between antibody and antigen was measured by a method called "ELISA" as shown in graph A in Figure 6.[29] The neutralizing antibodies, on the other hand, is measured via sVNT assay.[29] The neutralizing antibodies are crucial since having more capacity for neutralization may prevent the entrance of pathogens into the cells as well as stop the germs from changing their conformational shape.[30] All in all, all the data provided shows that the efficacy rate for mRNA vaccines which are BNT162b1 and mRNA-1273 is higher than the efficacy rates for an inactivated vaccine which is in this case CoronaVac (Sinovac).

At the moment, there are not any approved live-attenuated COVID-19 vaccines since they are still in the clinical trial process which makes it harder the comparison of live-attenuated vaccines to mRNA vaccines. However, logically, some reasoning for why live-attenuated vaccines cannot perform as effectively as mRNA vaccines on COVID-19 might be done. Most importantly, since live-attenuated vaccines contain the weakened version of a virus or a bacterium, they can only attack one specific virus or bacterium type meaning that whenever there is a new pathogenic agent, a new purification and testing process is required to develop a new vaccine.[1] On the other hand, mRNA vaccines can be standardized meaning that with minimal changes in the mRNA encoding different vaccines against different disease-causing microorganisms might be produced.[1] Additionally, because of this reason, using mRNA vaccines will increase the speed of the vaccine development process which is very necessary for outbreaks such as COVID-19.[1]

***Biosafety of Traditional and mRNA Vaccines:***

A final aspect that should be considered while comparing the advantages and disadvantages of traditional and mRNA vaccines is their biosafety. Most of the hesitance to getting injected with an mRNA COVID-19 vaccine comes from three points: the degree of degradation of DNA of the person, instability of mRNA, and side effects of the vaccine.[21,31] To begin with, mRNA COVID-19 vaccines cannot degrade the human genome (DNA) since mRNA does not enter the nucleus of the cells where DNA is located in each person and instead remains in the cytosol which is in the cytoplasm that is found outside

of the nucleus of the cells.[21] Moreover, mRNA is a molecule that breaks down readily in the human body that's the reason why self-amplifying mRNAs are used in mRNA COVID-19 vaccines to increase the amount of mRNA in the cells which will also augment the amount of antigen and therefore antibodies.[20] Secondly, the instability of mRNA is resolved due to the advancements in the delivery systems by using appropriate carriers in COVID-19 mRNA vaccines which helps to increase the safety of the vaccines.[21] The most commonly used carriers, today, for mRNA COVID-19 vaccines are lipid nanoparticles that belong to lipids which are one of the four organic compound types.[21] Therefore, they are biodegradable meaning that they are not harmful to human cells.[20] Moreover, they fuse with the phospholipid bilayer of human cells once the mRNA encapsulated in the lipid vehicle arrives at the target cell as was shown in Figure 5.[24] Lastly, the fear of side effects of the COVID-19 vaccine. mRNA vaccines indeed have side effects such as swelling, pain, redness where the shot was administered, headache, and fever.[32] Yet, these side effects are also available from conventional vaccines including live-attenuated and inactivated vaccines. In live-attenuated vaccines, especially, people are given the weakened version of the pathogen which increases the possibility of side effects in live vaccines since the substance given by the vaccine is the closest to the actual pathogenic agent.[33] Furthermore, in live-attenuated vaccines, there is the potential for reversion to natural virulence creating a very similar effect to the actual dreadful pathogen as a result of a secondary mutation of the attenuated microorganism.[18] Moreover, because of this reason, one important limitation of live-attenuated vaccines is that they cannot be injected into people with weak immune systems since the vaccine might produce the actual disease in the body.[18] On the other hand, inactivated vaccines do not possess the possibility of turning back to natural virulence.[18] Thus, people with weakened immune systems can get these vaccines.[18] However, for this type of vaccine, a minor fault in the bacteria culturing process might result in infections in the injected people.[34] Hence, special laboratory facilities that are very clean are required.[34] A final problematic situation with inactivated vaccines is that they might require adjuvants which is an ingredient used in vaccines to boost the vaccines such as aluminum hydrates.[35] This is a disadvantage for dead vaccines because adjuvants can cause more local reactions such as swelling and pain and systematic reactions such as fever and chills.[35] This means that inactivated vaccines in which adjuvants are present have more possibility of causing side effects compared to mRNA vaccines.

## Conclusion

In conclusion, several benefits of messenger ribonucleic acid (mRNA) vaccines are observed when compared to conventional vaccines comprising of live-attenuated vaccines and inactivated (dead) vaccines in manufacturing, efficiency, and biological safety. The main advantage of mRNA vaccines in production is the less requirement of time as opposed to classical vaccines which require more time due to the methods used in the discovery and development stage of the traditional vaccine development. When it comes to the efficacy of mRNA vaccines, even though previously, the instability of naked mRNA vaccines was causing a decrease in the efficiency of mRNA vaccines, the novel advancement in the technology allowed amelioration in the delivery systems which highly accelerated the augmentation of the efficacy of mRNA vaccines. Finally, the properties of mRNA as well as the technological advancement made the point of view toward mRNA vaccines more appealing. Based on these three-argument it can be concluded that mRNA vaccines provide multi-benefits over classical vaccines.

## References


1. Be unique, treat individualized. https://biontech.de/covid-19-portal/mrna-vaccines (accessed Jan 30, 2022).
2. Different types of vaccines. https://carrington.edu/blog/different-types-of-vaccines-2/ (accessed Jan 30, 2022).
3. A. Patricia Wodi, MD and Valerie Morelli, ba immunology https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/prinvac.pdf (accessed Jan 29, 2022).
4. Step T vaccine storage and handling. https://www.immunize.org/guide/pdfs/vacc-adults-step3.pdf (accessed Jan 29, 2022).
5. Types of vaccine. https://vk.ovg.ox.ac.uk/vk/types-of-vaccine (accessed Jan 29, 2022).
6. Content. https://vaccine-safety-training.org/inactivated-whole-cell-vaccines.html (accessed Jan 30, 2022).
7. Affairs, O. of R. Lyophilization of Parenteral (7/93). https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-guides/lyophilization-parenteral-793 (accessed Jan 29, 2022).
8. ACIP storage and handling guidelines for immunization. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/storage.html (accessed Jan 29, 2022).
9. Office of Infectious Disease and HIV/AIDS Policy (OIDP). Vaccine types. https://www.hhs.gov/immunization/basics/types/index.html (accessed Jan 29, 2022).
10. Dolgin, E. The tangled history of mrna vaccines. https://www.nature.com/articles/d41586-021-02483-w (accessed Jan 30, 2022).
11. Pardi, N.; Hogan, M. J.; Porter, F. W.; Weissman, D. MRNA vaccines - a new era in Vaccinology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5906799/ (accessed Jan 30, 2022).
12. What do we know about the mrna vaccine and cytokine storm? https://health-desk.org/articles/what-do-we-know-about-the-mrna-vaccine-and-cytokine-storm (accessed Jan 30, 2022).
13. Kowalzik, F.; Schreiner, D.; Jensen, C.; Teschner, D.; Gehring, S.; Zepp, F. MRNA-based vaccines. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8103517/ (accessed Jan 30, 2022).
14. J, L. I. The emergence of inactivated vaccines: Bharat Biotech. https://www.bharatbiotech.com/blog/the-emergence-of-inactivated-vaccines/ (accessed Jan 30, 2022).
15. Vaccine development, testing, and regulation. https://www.historyofvaccines.org/content/articles/vaccine-development-testing-and-regulation (accessed Jan 30, 2022).
16. voxdotcom. MRNA vaccines, explained. https://www.youtube.com/watch?v=mvA9gs5gxNY (accessed Jan 30, 2022).
17. The fastest vaccine in history. https://connect.uclahealth.org/2020/12/10/the-fastest-vaccine-in-history/ (accessed Jan 30, 2022).
18. Attenuated vaccine. https://www.sciencedirect.com/topics/immunology-and-microbiology/attenuated-vaccine (accessed Jan 30, 2022).
19. Hajj, K. A.; Whitehead, K. A. Tools for translation: Non-viral materials for therapeutic mrna delivery. https://www.nature.com/articles/natrevmats201756 (accessed Jan 30, 2022).
20. How does a mrna vaccine compare to a traditional vaccine?



DOI: 10.36838/v4i4.5

https://www.vumc.org/viiii/infographics/how-does-mrna-vaccine-compare-traditional-vaccine (accessed Jan 30, 2022).
21. Liang, Y.; Huang, L.; Liu, T. Development and delivery systems of mrna vaccines. https://www.frontiersin.org/articles/10.3389/fbioe.2021.718753/full (accessed Jan 30, 2022).
22. Nayerossadat, N.; Maedeh, T.; Ali, P. A. Viral and nonviral delivery systems for gene delivery. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3507026/ (accessed Jan 30, 2022).
23. Sanders, N. N. Low-dose single-shot covid-19 mrna vaccines lie ahead. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8134890/#:~:text=Currently%20the%20COVID%2D19%20mRNA,at%20least%20six%20times%20faser. (accessed Jan 30, 2022).
24. Anand, P.; Stahel, V. P. Review the safety of covid-19 mrna vaccines: A Review. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8087878/ (accessed Jan 30, 2022).
25. Baden, L. R.; El Sahly, H. M.; Essink, B.; Kotloff, K.; Frey, S.; Novak, R.; Diemert, D.; Spector, S. A.; Rouphael, N.; Creech, C. B.; McGettigan, J.; Khetan, S.; Segall, N.; Solis, J.; Brosz, A.; Fierro, C.; Schwartz, H.; Neuzil, K.; Corey, L.; Gilbert, P.; Janes, H.; Follmann, D.; Marovich, M.; Mascola, J.; Polakowski, L.; Ledgerwood, J.; Graham, B. S.; Bennett, H.; Pajon, R.; Knightly, C.; Leav, B.; Deng, W.; Zhou, H.; Han, S.; Ivarsson, M.; Miller, J.; Zaks, T.; COVE Study Group. Efficacy and safety of the mrna-1273 SARS-COV-2 vaccine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7787219/ (accessed Jan 30, 2022).
26. Fadlyana, E.; Rusmil, K.; Tarigan, R.; Rahmadi, A. R.; Prodjosoewojo, S.; Sofiatin, Y.; Khrisna, C. V.; Sari, R. M.; Setyaningsih, L.; Surachman, F.; Bachtiar, N. S.; Sukandar, H.; Megantara, I.; Murad, C.; Pangesti, K. N. A.; Setiawaty, V.; Sudigdoadi, S.; Hu, Y.; Gao, Q.; Kartasasmita, C. B. A phase III, observer-blind, randomized, placebo-controlled study of the efficacy, safety, and immunogenicity of SARS-COV-2 inactivated vaccine in healthy adults aged 18-59 years: An interim analysis in Indonesia. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8461222/ (accessed Jan 30, 2022).
27. CoronaVac efficacy data from Turkey. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02288-1/fulltext (accessed Jan 30, 2022).
28. Ranzani, O. T.; Hitchings, M. D. T.; Dorion, M.; D'Agostini, T. L.; de Paula, R. C.; de Paula, O. F. P.; Villela, E. F. de M.; Torres, M. S. S.; de Oliveira, S. B.; Schulz, W.; Almiron, M.; Said, R.; de Oliveira, R. D.; Vieira da Silva, P.; de Araújo, W. N.; Gorinchteyn, J. C.; Andrews, J. R.; Cummings, D. A. T.; Ko, A. I.; Croda, J. Effectiveness of the CORONAVAC vaccine in older adults during a gamma variant associated epidemic of covid-19 in Brazil: Test negative case-control study. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8377801/ (accessed Jan 30, 2022).
29. Supplementary appendix - thelancet.com. https://www.thelancet.com/cms/10.1016/S2666-5247(21)00177-4/attachment/ea575ee3-b3a2-4ec9-b361-303fed53d75e/mmc1.pdf (accessed Jan 30, 2022).
30. Zoppi, L. What are neutralizing antibodies? https://www.news-medical.net/health/What-are-Neutralizing-Antibodies.aspx#:~:text=Neutralizing%20antibodies%20can%20also%20stop,the%20harmful%20effects%20of%20toxins. (accessed Jan 30, 2022).
31. Watch out for misinformation about mrna and inactivated virus COVID-19 vaccines. https://www.gov.sg/article/watch-out-for-misinformation-about-mrna-and-inactivated-virus-covid-19-vaccines (accessed Jan 30, 2022).
32. Katella, K. Comparing the COVID-19 vaccines: How are they different? https://www.yalemedicine.org/news/covid-19-vaccine-comparison (accessed Jan 30, 2022).
33. Possible side effects from vaccines. https://www.cdc.gov/vaccines/vac-gen/side-effects.htm (accessed Jan 30, 2022).
34. The different types of covid-19 vaccines. https://www.who.int/news-room/feature-stories/detail/the-race-for-a-covid-19-vaccine-explained (accessed Jan 30, 2022).
35. Adjuvants and vaccines. https://www.cdc.gov/vaccinesafety/concerns/adjuvants.html (accessed Jan 30, 2022).

## Authors

Deniz Cenikli is a sophomore student at Uskudar American Academy in Turkey. She is currently in the IB diploma program. She immersed herself in biology, chemistry, and mathematics. As a student willing to study medicine, she is eager to enhance her scientific knowledge.