



Review on Various Type of Vaccines for Controlling Infectious Disease

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Abstract

Background: Vaccines have played a critical role in the prevention and treatment of infectious diseases, greatly lowering worldwide morbidity and mortality. This review examines many forms of vaccinations. In contrast, inactivated vaccines, such as the polio vaccine, are safer for immune compromised people, they frequently require booster shots.

Aim: This review emphasises the importance of vaccinations in public health and the need for innovation to tackle future infectious disease threats. The introduction of new pathogens has prompted the creation of novel vaccination platforms, including mRNA and viral vector vaccines. mRNA vaccines, such as those used to treat COVID-19, use genetic instructions to direct cells to manufacture antigens, resulting in strong immunity.

Conclusion: These vaccines have demonstrated excellent efficacy and rapid scaling, making those valuable instruments in pandemics. This review emphasises the necessity of designing vaccine methods that meet individual illnesses, demographics, and logistical obstacles. While vaccinations have considerably reduced the occurrence of infectious diseases, more research is needed to address future threats, improve vaccine efficacy, and overcome obstacles such as vaccine reluctance and global inequities. Understanding the capabilities and limits of each vaccine type will help researchers and policymakers better equip healthcare systems to address current and future infectious disease concerns.

Keywords: Vaccines; Infectious Disease; COVID-19; Nanoparticle

Abbreviations

SARS-COV-2: Severe Acute Respiratory Syndrome Coronavirus 2; COVID-19: Coronavirus Disease 2019; WHO: World Health Organisation; VLPs: Virus-like Particles; CDCP: Centres for Disease Control and Prevention; DALYs: Disability-Adjusted Life Years; NPs: Nanoparticles; PAMPs: Pathogen Associated

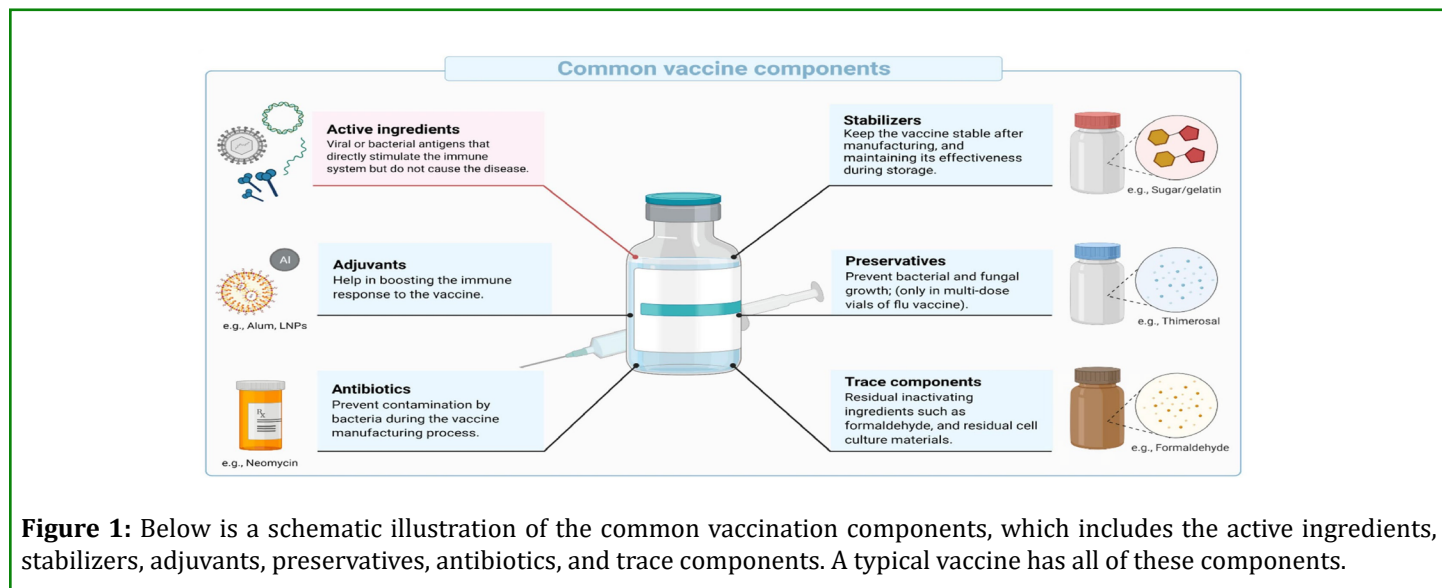
Molecular Patterns; UNICEF: United Nations Children's Fund; CEPI: Coalition for Epidemic Preparedness Initiative.

Introduction

Microorganisms that are considered to be pathogenic, such as bacteria, viruses, parasites, and fungi, are responsible

for the development of infectious diseases that can be transmitted from one person to another, either directly or indirectly. Infectious diseases are the greatest cause of death around the globe. Every year, around twenty million people are affected by measles, the most of whom are found in developing countries in Asia and Africa. In the 20th century, the disease known as smallpox was responsible for the deaths of between 300 and 500 million people [1]. The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is responsible for the pandemic caused by the coronavirus disease 2019 (COVID-19), rapidly spread around the world within a span of six months. It displayed heightened fatality rates among persons who were aged and those who had comorbidities. Because of the epidemic, the economy of the entire world has been severely impacted. A succession of insufficient and restrictive mitigation measures, such as social distancing, mask-wearing, travel limitations, and the avoidance of gatherings, have been the sole means of control that has been used in the absence of lockdowns. Given that more than 100 million people are sick and more than 2 million have passed away as a result of the pandemic, including vaccinations into the existing countermeasures

appears to be the most promising option for containing the epidemic [2]. The cumulative effect of these elements necessitates that researchers and policymakers maintain vigilance, reevaluate existing approaches to monitoring and controlling emerging infectious disease threats, and rethink global frameworks for the management of pandemics. Vaccines are biological substances that are designed to stimulate and condition the immune system in preparation for the fight against illnesses or infections. For the purpose of recognizing, responding to, and remembering illnesses, they are dependent on the complex immune system of mammals. The most important components of vaccinations are antigens that are either bio-manufactured or obtained from the organism that is being protected against. There is a possibility that the remaining components from the manufacturing process, as well as preservatives, stabilisers, and excipients, will be included. It is common practice to utilise adjuvants in order to improve immunogenicity and efficacy in specific populations, such as neonates, the elderly, and individuals who are immunocompromised. Adjuvants also facilitate antigen dose sparing, which helps to expand the global supply of vaccinations [3].



There is a major influence that vaccination has on the health of the population all over the world. There is no other method that has had such a substantial impact on the decrease of mortality and the increase in population levels, with the exception of the provision of potable water. The development of vaccines that are both safe and effective against diseases that are responsible for a large amount of morbidity and death is one of the most significant scientific achievements of the twenty-first century. In addition to sanitation and the provision of safe drinking water, vaccination is one of the public health measures that has unquestionably contributed to an improvement in health outcomes all around the world.

The use of vaccines is estimated to have prevented six million deaths annually from diseases that may have been prevented by vaccination [4]. One of the most efficient ways to protect oneself against infectious diseases is through vaccination. The process of administering a biological substance to the immune system of a receiver in order to stimulate the formation of antibodies or other alterations that will provide future protection against particular infectious diseases is referred to as vaccination [5]. The vaccination process is widely considered to be the most successful and cost-effective medical intervention that has ever been established. Vaccination can be produced from living modified organisms,

creatures that have been inactivated or dead, extracted cellular fractions, toxins, or a combination of these several types [6].

History of Vaccine for Controlling Infectious Disease

Edward Jenner, who lived in the 18th century, is credited with coining the term “vaccine,” despite the fact that inoculation practices extend back more than 500 years. It is traced back to the Latin term *vacca*, which literally translates to “cow.” From the hands of milkmaids in the year 1796, Jenner infected a child who was eight years old with cowpox lesions. Immunity to smallpox was ultimately achieved as a result of this. After a period of eighty years, Louis Pasteur played a significant role in the development of a live attenuated rabies vaccination for humans that were extremely efficient. The discovery of a number of microorganisms by Koch in the nineteenth century was a significant event that contributed to the development of germ theory [7]. This era witnessed the introduction of innovative pathogen vaccinations in addition to significant research being conducted all around the world. Up to 1930, vaccines against rabies, typhoid fever, diphtheria, TB, tetanus, and pertussis were created and put on the market [8,9]. A new era of mass vaccine production began in 1931, according to the key finding that Louis Pasteur made on the propagation of the virus in chicken embryos. This new age of vaccine production utilised a mix of processes. Between the years 1930 and 1950, and especially during World War II, the military’s objectives served as a significant source of impetus for vaccine research. Furthermore, from that moment onwards, significant money was provided by foundations and state institutions such as the World Health Organization (WHO) and research institutes. The development of vaccines against diseases such as influenza, Japanese encephalitis B, and polio occurred during this time period. Following the conclusion of World War II, targeted immunisation initiatives emerged as a universal method for enhancing the health of the general population [10]. Over twenty different vaccinations against infectious diseases are currently being administered to a large number of people all over the world in order to avoid human infections. This is a noteworthy finding; nevertheless, when compared to the amount of infectious diseases that are currently affecting humans and animals all over the world, it highlights significant knowledge gaps in particular pathogens, immunopathology, and the intricate relationship that exists between pathogens and hosts. As a consequence of this, there are number of diseases that are widespread around the world, despite the fact that there is not yet a vaccine that is effective, nor is there even a pre-clinical or clinical trial that is now being conducted [11]. In the course of the COVID-19 pandemic, vaccinations based on nucleic acids were the most cutting-edge and forward-thinking innovations in the field of vaccine development. The mRNA-based coronavirus vaccine

that was developed by Pfizer and Moderna and released near the end of the year 2020 is widely recognized as one of the most significant advancements in the field of vaccine research. The fact that vaccinations based on mRNA were used all around the world during the pandemic provided evidence of the safety and dependability of the technology. This is significant because it illustrates that the general public is willing to support technological advancements and it promotes additional research and development in the field of mRNA-based immunisations. Unexpectedly, this approach has emerged as a significant component in the process of vaccine development [12].

Types of Vaccines

Inactivated vaccines: A number of vaccines, including those for influenza, cholera, polio, bubonic plague, hepatitis A, and rabies, contain germs that have been rendered inactive but were formerly very infectious. These microorganisms have been eradicated through the use of chemicals, heat, radiation, and antibiotics [13].

DNA Vaccines: As an illustration, ongoing Phase 2/3 trials such as GX-19 (Genexine, Inc.) and INO-4800 (International Vaccine Institute; Inovio Pharmaceuticals) Canada—COVID-19 Symvivo (AnGes, Inc.) are examples of such trials. Plasmids have the ability to reach the nuclei of B cells, which is necessary for the production of RBD antibodies or S proteins. This type of DNA vaccination has a number of advantages, including the ability to be freeze-dried, kept for an extended period of time, and transmitted at room temperature (in contrast to ultra-fragile mRNA vaccines), as well as the elimination of the requirement to carry the live virus throughout the preparation process. There are some plasmid-derived DNA vaccines that do not yet have a general use license, despite the fact that they are now in phase 3 testing. Currently, the only application of DNA vaccines that is approved is in the veterinary sector [14].

Live-Attenuated, or Replication-Competent Attenuated Vaccines: These vaccines, which are also known as replication-competent attenuated vaccines or live attenuated vaccines, are manufactured from viruses that have been weakened, which means that the virulence of the disease has been greatly reduced. However, the attenuated viruses are still capable of infecting, multiplying, and releasing themselves within the host the same way that a true infection would. The capability of this technology to maintain the viruses’ capacity for replication without causing disease or a return to infectiousness is an essential component in the creation of this technology [15].

Virus-like Particles (VLPs) Vaccines: Virus-like particles, also known as VLPs, are collections of macromolecules that

are designed to resemble a native virus in terms of their size, structure, and surface epitopes. VLPs can be characterized according to the amount of protein layers that make up the rigid structure known as the capsid and whether or not a lipid envelope is present [16]. VLP-derived vaccines are often manufactured in bioreactors after the transfection of insect, yeast, bacterial, plant, or mammalian cells with one or more genetic constructs. This process can vary from organism to organism. The constructions encode at least two structural features of the original virus, which enables the virus to self-assemble into particles that are incapable of replicating itself [17]. To increase the immunogenicity of VLPs throughout the design and production stages, it is possible to make use of a variety of techniques, including the incorporation of immunogenic or dominant peptides and/or adjuvants, surface chemical modifications, and the selection of the VLP system. Repurposing the technology for a variety of applications, such as chemical catalysis, imaging (such as positron emission tomography and magnetic resonance imaging), and targeted drug or nucleic acid delivery, is made possible by targeted surface modifications that involve straightforward chemical processes. These modifications increase the potency of the technology, alter its tropism, and make it possible to repurpose it [18].

Why Vaccines is Important for Chronic and Acute Diseases

The World Health Organization (WHO) has just issued a recommendation for the use of this vaccine in baby immunisation programs all over the world. It is expected that a successful immunisation program that achieves a high coverage rate would also reduce the spread of infectious agents. This will lead to herd immunity, which will boost the overall impact of the program. It would appear that this form of vaccine would be very desirable for the purpose of preventing infections that eventually lead to the several types of chronic illnesses that bacteria are capable of causing, which indicates that multiple immunisation strategies will be required. The treatment of the persistent infection and the prevention of the initial acute infection are the two primary categories that can be used to classify these.

It is possible to get several benefits from the avoidance of acute infections. The concept of vaccination as it is currently understood would be consistent with this. The process of developing a vaccine would be straightforward up until and including the clinical efficacy study, which would evaluate the effectiveness of the vaccine in preventing acute infections. As a consequence of this, there is no need to be concerned about the pathophysiology of the chronic disease. In the case of the hepatitis B vaccine, this approach has been shown to be effective, as evidenced by a reduction in the incidence of chronic hepatitis and liver cancer ten years following

vaccination in infants. In the event that a connection to the infectious agent is proven and a vaccination is available, the chronic disease can be diagnosed quite early in life, such as in the case of diabetes in children [19]. In accordance with the World Health Organization (WHO), a chronic disease is defined as a condition that persists for an extended period of time, advances gradually, and cannot be passed on from one individual directly to another. Every year, chronic illnesses claim the lives of 38 million additional people. In spite of the fact that addiction, arthritis, autism, osteoporosis, and different psychiatric disorders are considered chronic conditions that affect thousands of adults each year, the Centres for Disease Control and Prevention (CDC) does not suggest any vaccines directed specifically towards individuals who suffer from these conditions. It is important for those who are afflicted with these problems to visit their physician regarding the vaccinations that are suitable for their way of life. According to the World Health Organisation (WHO), non-communicable diseases can be broken down into four distinct categories: cardiopulmonary disease (which accounts for 17.5 million deaths annually), cancer (8.2 million), chronic respiratory disease (4 million), and diabetes (1.5 million). It is recommended by the Centres for Disease Control and Prevention (CDC) that individuals who have these disorders have additional immunisations. This is due to the potential implications that may arise when both the chronic disease and the vaccine-preventable disease are present within the body [20].

Reduction in Infectious Diseases Morbidity and Mortality

The prevention of morbidity and mortality caused by serious diseases that disproportionately affect children has been the most significant impact that vaccines have had a substantial impact on. The use of vaccines is expected to save 386 million life years and 96 million disability-adjusted life years (DALYs) across the world. Additionally, vaccines are responsible for preventing almost six million deaths annually. Some of the conventional methods for evaluating the impact of vaccinations include the following: vaccine efficacy, which refers to the direct protection that is provided to a vaccinated group under optimal conditions, such as trial settings; or vaccine effectiveness, which refers to the direct and indirect influence that vaccines have on the population in a normal context. Therefore, in order to provide a quantifiable measure of the impact of vaccines, it is necessary to estimate the extent of the morbidity and mortality that is prevented. The most significant contribution that vaccines have made to the reduction of morbidity and mortality from serious illnesses that disproportionately afflict children is the use of vaccines. It is estimated that immunisations save approximately six million lives per year, in addition to 386 million life years, 96 million disability-adjusted life years (DALYs), and disability-

adjusted life years (DALYs). Under ideal conditions, such as those found in clinical trials, the term “vaccine efficacy” refers to the direct protection that is delivered to a group of individuals who have been vaccinated. On the other hand, the term “vaccine effectiveness” refers to the direct and indirect influence that immunisations have on the population in a situation that is taking place in the real world. Therefore, in order to offer a numerical estimate of the impact of vaccines, it is required to measure the amount of morbidity and mortality that is avoided after vaccination [21].

Role of Nanoparticles in Vaccines Development

To a greater extent than any other type of nanomaterial, nanoparticles (NPs) have been employed in the creation of vaccination applications. Vaccine delivery nanoparticles typically consist of three components: the material or materials that make up the nanoparticle, which may include natural or synthetic polymers, inorganic substances, lipids, and so on; immunogen or immunomodulatory agents, which may include DNA vaccines, siRNA, cytokines, and so on; and, finally, targeting and immunostimulatory ligands that are added to the surface of the nanoparticle, which may include tissue-specific ligands, immune-specific ligands, pathogen associated molecular patterns (PAMPs), and etc. Transportation, intracellular trafficking, cellular absorption, as well as the biodegradability and biocompatibility of the nanoparticles (NPs) are all important tasks that are performed by the material composition of particles [22]. There is a great deal of potential for the production of vaccinations of the next generation through the use of nanoparticles that have been coated with antigens and adjuvants. Because of the improved stability, immunogenicity, and targeting potential of these coated nanoparticles, the immune system is able to respond more effectively to a wide variety of infections and cancers. The field of immunisation is seeing the development of vaccines that are coated with nanoparticles. Recent studies that are presented here highlight the growing popularity of vaccinations that are coated with nanoparticles and provide valuable insights into the design and development of vaccines in the future. When it comes to the production of COVID-19 vaccines, Smith et al. describe the utilisation of lipid-based nanoparticles that have been coated with viral antigens. It is demonstrated by the author that these coated nanoparticles generate powerful immunological responses, such as the creation of neutralising antibodies and the activation of T-cells, which ultimately results in improved protection against SARS-CoV-2 infection [23]. Within the context of another work, Johnson et al. discuss the utilisation of polymer-coated nanoparticles for the purpose of developing a vaccine against malaria. In preclinical models, the researchers demonstrate that these coated nanoparticles are capable of successfully delivering several antigen components, which results in a powerful immune response

and protection against Plasmodium falciparum infection that is long-lasting [24].

Impact of Vaccine in Community Health

It is difficult to overstate the fact that vaccination has a significant impact on the health of people all over the world. Other than the provision of safe water, no other method has been shown to have such a significant impact on the decrease of mortality and the expansion of the population [25]. The development of vaccines that are both safe and effective against diseases that are responsible for a large amount of morbidity and death is one of the most significant scientific achievements of the twenty-first century. In addition to sanitation and the provision of safe drinking water, vaccination is one of the public health measures that have unquestionably contributed to an improvement in health outcomes all around the world. There is a belief that vaccines have prevented six million deaths annually from diseases that may have been prevented by vaccination [26]. By the year 2055, it is anticipated that the global population will be close to 10 billion people [27]. This is a direct result of the development of effective vaccines that lower the risk of disease and raise the average life expectancy across all continents. However, there is still a great deal of effort to be done in order to ensure that vaccines are funded, supplied, distributed, and administered to all populations. This is especially true for populations who are difficult to reach, such as those who question the protective advantage of vaccines and those who reside in areas where there is civil unrest. The various funding streams of organizations such as the World Health Organization (WHO), the United Nations Children’s Fund (UNICEF), Gavi, the Vaccine Alliance, the Bill & Melinda Gates Foundation, and the Coalition for Epidemic Preparedness Initiative (CEPI) have made it possible to expand the benefits of vaccines to everyone. This has been made possible by the expansion of vaccine benefits. During the 2019 SARS-CoV-2 pandemic, the role of these groups in international collaboration and involvement was vital. This is because the COVID-19 pandemic had a significant impact on the health and finances of societies in high-, middle-, and low-income nations. Within the scope of this assessment, the advantages of vaccinations with regard to health, the economy, and the social fabric will be underlined. It is imperative that these aspects be taken into consideration throughout the comprehensive impact assessment in order to guarantee that those who are responsible for determining funding priorities give vaccines the highest priority [28].

Conclusion

Due to the fact that vaccines have been able to successfully prevent and treat a wide variety of infectious diseases, the health of people all over the world has considerably

improved. The burden of disease and the death rate have both been significantly reduced thanks to the significant contributions provided by conventional live-attenuated and inactivated vaccines, as well as novel mRNA and viral vector platforms. These numerous vaccination strategies meet the specific challenges that are presented by a variety of diseases and target populations in order to guarantee that immune responses are both tailored and effective. The development of mRNA vaccines brought about a revolution in the field of immunisation technology, as evidenced by the fact that these vaccines were successful in combating Covid-19. As a result of their high level of effectiveness and rapid development, they demonstrate considerable potential as a method for combating newly emerging infectious illnesses. In a manner analogous to this, viral vector vaccines have shown tremendous promise by combining potent immune activation with safety, particularly in cases involving outbreaks. Despite these improvements, there are still issues that need to be addressed. These issues include a reluctance to receive the vaccination, restricted access in regions with limited resources, and the advent of variants that could reduce the effectiveness of the vaccine. In order to address these issues and enhance the stability, storage, and delivery of vaccines, it is necessary to engage in international collaboration, implement equitable distribution techniques, and implement continual innovation. In conclusion, the development of vaccinations highlights the significant role that scientific innovation plays in the protection of public health. The availability of a wide range of vaccine types ensures that they can be adapted to a number of diseases and situations, while ongoing research works to eliminate the limits that are currently in place. Vaccines will continue to be a vital instrument for the prevention of disease, the saving of lives, and the promotion of global health security as the world continues to face new infectious dangers. Increasing public trust and making sure that everyone has equal access will be absolutely necessary in order to make the most of the benefits that these life-saving therapies have to offer.

References

- Baafi J, Darko IO, Asenso FW (2017) Vaccination as a control of infectious diseases. *J Appl Computat Math* 6(3): 1-8.
- Excler JL, Saville M, Berkley S, Kim JH (2021) Vaccine development for emerging infectious diseases. *Nature medicine* 27(4): 591-600.
- Ghattas M, Dwivedi G, Lavertu M, Alameh MG (2021) Vaccine technologies and platforms for infectious diseases: Current progress, challenges, and opportunities. *Vaccines* 9(12): 1490.
- Rodrigues CM, Plotkin SA (2020) Impact of vaccines; health, economic and social perspectives. *Frontiers in microbiology* 11: 1526.
- Elochukwu IC, Okoro O, Unekwe P, Irinmwinnuwa E (2020) role of vaccines in prevention of diseases: a review. *Longdom Publishing SL* 12(1).
- Berkeley S (2014) improving access to vaccine through tiered piercing. *Lancet* 383(9936): 2265-2267.
- Saleh A, Qamar S, Tekin A, Singh R, Kashyap R (2021) Vaccine development throughout history. *Cureus* 13(7): e16635.
- Wever PC, Bergen L (2012) Prevention of tetanus during the First World War. *Med Humanit* 38(2):78-82.
- Rappuoli R, Malito E (2014) History of Diphtheria Vaccine Development. *Corynebacterium diphtheriae* and Related Toxigenic Specie. Springer pp: 225-238.
- Tahamtan A, Charostad J, Shokouh SJ, Barati M (2017) An overview of history, evolution, and manufacturing of various generations of vaccines. *Journal of Archives in Military Medicine* 5(3).
- Silva FC, Luca PM, Lima-Junior JD (2023) Vaccine development against infectious diseases: state of the art, new insights, and future directions. *Vaccines* 11(11): 1632.
- Kumar R (2024) New trends in vaccine characterization, formulations, and development. *Vaccines* 12(3): 338.
- Shapiro CG, Kendrick P, Grace E (2010) Pertussis vaccines emerging infectious. *Journal of medicine* 339(4): 209-215.
- Lotfi H, Mazar MG, Ei NM, Fahim M, Yazdi NS (2023) Vaccination is the most effective and best way to avoid the disease of COVID-19. *Immunity, Inflammation and Disease* 11(8): e946.
- Mak TW, Saunders ME (2006) 23-Vaccines and Clinical Immunization. In: Mak TW, Saunders ME (Eds.), *The Immune Response*. Academic Press USA, pp: 695-749.
- Nooraei S, Bahrulolum H, Hoseini ZS, Katalani C, Hajizade A, et al. (2021) Virus-like Particles: Preparation, immunogenicity and their roles as nanovaccines and drug nanocarriers. *J Nanobiotechnology* 19: 59.
- Ding X, Liu D, Booth G, Gao W, Lu Y (2018) Virus-like Particle Engineering: From Rational Design to Versatile Applications. *Biotechnol J* 13(5): e1700324.
- Lua LHL, Connors NK, Sainsbury F, Chuan YP, Wibowo

- N, et al. (2014) Bioengineering Virus-like Particles as vaccines. *Biotechnol Bioeng* 111(3): 425-440.
19. Mäkelä PH (2004) The Infectious Etiology of Chronic Diseases: Defining the Relationship, Enhancing the Research, and Mitigating the Effects: Workshop Summary, National Academies Press, pp: 175.
20. Smith K (2017) Vaccines and chronic disease. *Delaware Journal of Public Health* 3(1): 46.
21. Rodrigues CM, Plotkin SA (2020) Impact of vaccines; health, economic and social perspective. *Frontiers in microbiology* 11: 1526.
22. Hajizade A, Ebrahimi F, Salmanian AH, Arpanaei A, Amani J (2014) Nanoparticles in vaccine development. *Journal of Applied Biotechnology Reports* 1(4): 125-134.
23. Nooraei S, Bahrulolum H, Hoseini ZS, Katalani C, Hajizade A, et al. (2021) Virus-like particles: preparation, immunogenicity and their roles as nanovaccines and drug nanocarriers. *J Nanobiotechnology* 19(1): 59.
24. Ielo I, Rando G, Giacobello F, Sfameni S, Castellano A, et al. (2021) Synthesis, chemical–physical characterization, and biomedical applications of functional gold nanoparticles: A review. *Molecules* 26(19): 5823.
25. Pollard AJ, Perrett KP, Beverley PC (2009) Maintaining protection against invasive bacteria with protein-polysaccharide conjugate vaccines. *Nat Rev Immunol* 9(3): 213-220.
26. Poovorawan Y, Chongsrisawat V, Theamboonlers A, Leroux-Roels G, Kuriyakose S, et al. (2011) Evidence of protection against clinical and chronic hepatitis B infection 20 years after infant vaccination in a high endemicity region. *J Viral Hepat* 18(5): 369-375.
27. Riumallo-Herl C, Chang AY, Clark S, Constenla D, Clark A, et al. (2018) Poverty reduction and equity benefits of introducing or scaling up measles, rotavirus and pneumococcal vaccines in low-income and middle-income countries: a modelling study. *BMJ Glob Health* 3(2): e000613.
28. Soergel P, Makowski L, Schippert C, Staboulidou I, Hille U, et al. (2012) The cost efficiency of HPV vaccines is significantly underestimated due to omission of conisation-associated prematurity with neonatal mortality and morbidity. *Hum Vacc Immunother* 8(2): 243-251.