IOSR Journal Of Pharmacy
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 11, Issue 2 Series. I (February 2021), PP. 10-28
www.iosrphr.org

Breakthrough that change patients lives Clinical Study design of pfizer-BionTech COVID-19 vaccine Pictorial Representation of BNT162b2 (tozinameran).

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Received 29 January 2021; Accepted 13 February 2021

Abstract: The pandemic has drawn focus to the need for greater racial and ethnic diversity in Clinical trials. This is not a new issue diverse communities have long been underrepresented in clinical research but COVID-19 has put a necessary spotlight on the work to do. This Pictorial representation may guide to design clinical data.
Keywords: Clinical Study Design, Pfizer-BionTech COVID-19 vaccine, pictorial Representation

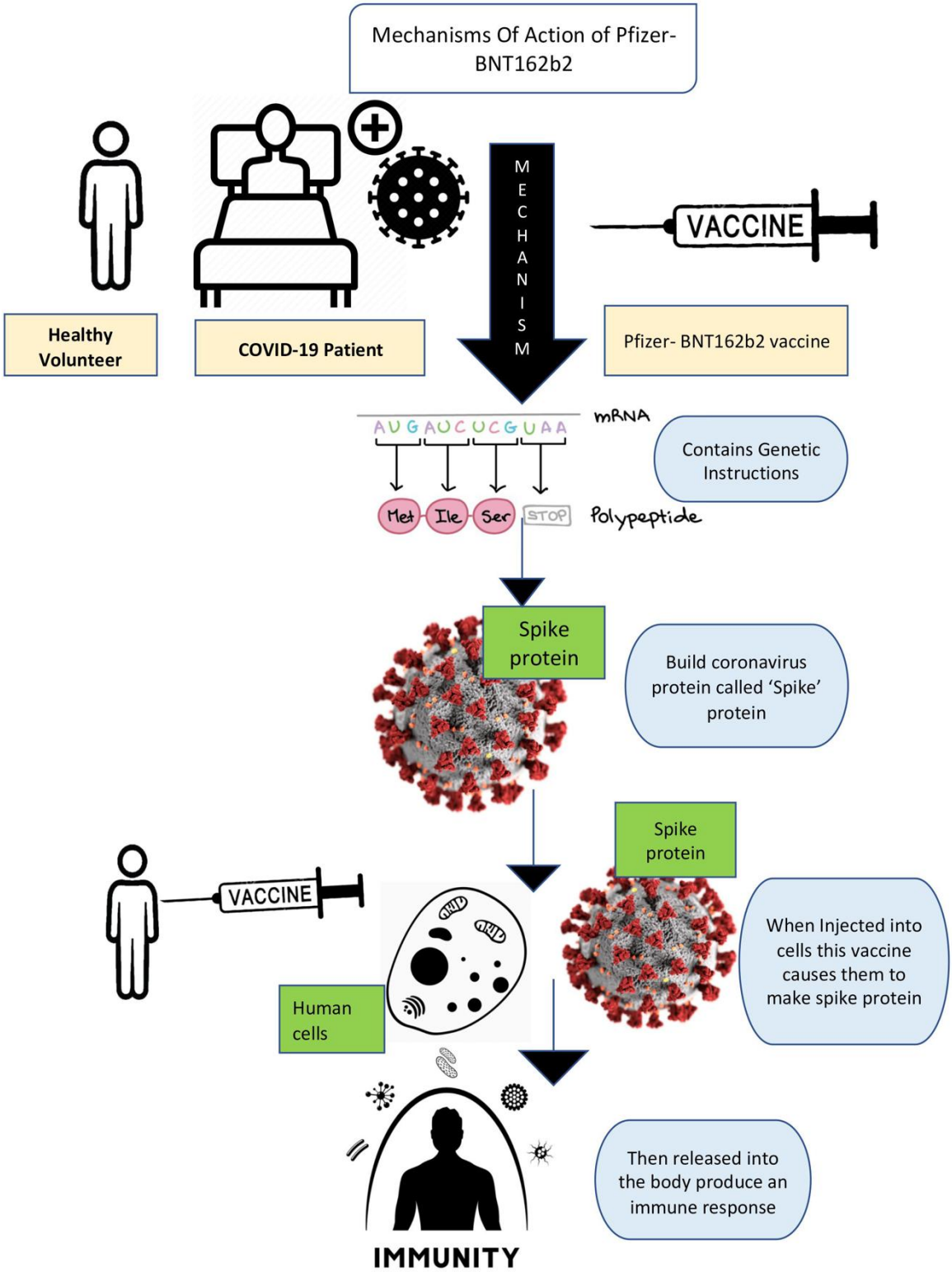
I. INTRODUCTION:

- the Covid-19 pandemic started, the community has come together to work on potential treatments and vaccines.
- As a part of this effort, tele health are being explored, including one based on messenger RNA, also known as mRNA.
- Currently, this technologies are being used to research a new type of vaccine to determine whether it may be able to help fight COVID-19 disease.
- There are many distinct types of vaccines used to help prevent infections, all of which have the same target to instruct your immune system to recognize and fight against infectious disease.
- mRNA vaccines are not made up of the actual pathogen. They contain genetic codes about the pathogen, that they don't contain weakened, dead or non infectious parts of a virus.
- Scientist identified a coronavirus protein, the spike protein, that the virus uses to attack our cells.

- If we could "instruct" the body to recognise and block the virus spike protein interaction of a virus infected cell,
- Then it may be possible to protect an individual from disease.
- mRNA vaccines are designed to instruct your body's cells to make a spike protein, known as antigen , which could potentially instruct your immune system to recognize and fight the virus without exposing you to the real thing.
- Our immune system recognizes this antigen as a signal of a foreign invader and summons its defences, like antibodies and T-cells.
- When the real virus comes, scientist believe that our immune system could recognize the virus spike proteins and prepare to defend against infection and illness.
- Because a vaccinated person may not experience the virus for sometime after vaccination, the goal is to instruct memory cells so that they can quickly respond to a potentially invasion.
- Clinical trials are being run to confirm efficacy and safety of this process.
- This work my help provide protection against COVID-19 disease.
- Scientist moved forward for mRNA vaccine, because of the anticipated time to develop and manufacture them is quick.
- We don't need the actual virus to create an mRNA vaccine. we only need a small piece of its genetic code.
- It is also believed and continue to be studied, that mRNA vaccines may be given multiple times, and these will "boosts" to the immune system may help to increase immunity.
- This work that's happening now has been years in the making: BionTech has been developing proprietary mRNA technology for more than a decade and is supported by Pfizer's global vaccine development and manufacturing capabilities.
- Scientist have been working jointly with clinical researchers and drug regulatory agencies to evaluate the efficacy and safety of vaccine candidate and continue to observe high scientific and ethical standards, regarding the conduct of clinical trials and the efficacy vaccine results.
- This includes large scale clinical research, such as clinical study design through feedback from drug regulatory bodies, independent safety monitors and subject matter experts, enrolling up to 10,000 participants in a clinical study.
- Research is determined the safety and efficacy of mRNA vaccine candidates.
- Science has overcome disease before, and it will again.
- Scientist hope that mRNA vaccines become one of the tools in the fight against COVID-19.
- Moving at a speed of Science Pfizer and BionTech recently announced interim efficacy results from the late stage study of their potential Covid-19 vaccine. However, effectiveness is only one of the three requirements and, alone is not enough for us to apply regulatory authorisation. They have been generating safety data from thousands of trial participants. And there are providing data confirming there vaccine candidate can be consistently can be consistently manufactured to meet high quality standards. Assuming positive data across efficacy, safety and manufacturing standards, pfizer they applied for regulatory authorisation in the US, UK and other countries.
- They remain committed to moving at the speed of Science and only delivering a potential vaccine to the speed of Science and only delivering a potential vaccine to the world. They have demonstrated success in all 3 key areas:

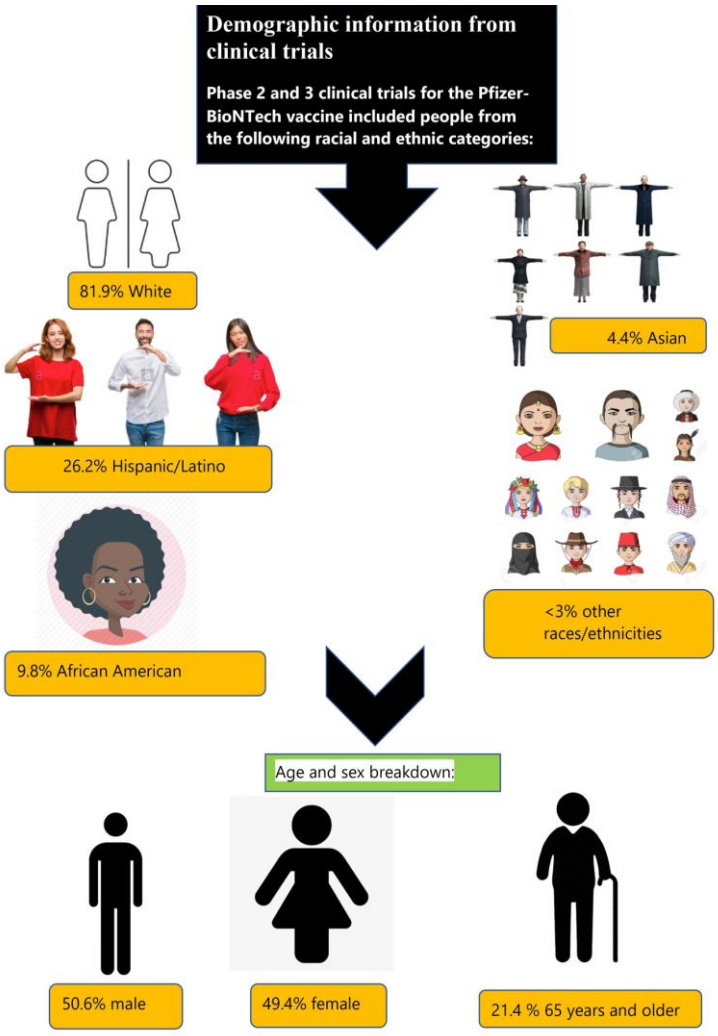
1) Evidence of efficacy in the appropriate number of vaccinated patients.
2) Evidence of safety with data from thousands of people.
3) Manufacturing consistently to the highest quality standards.

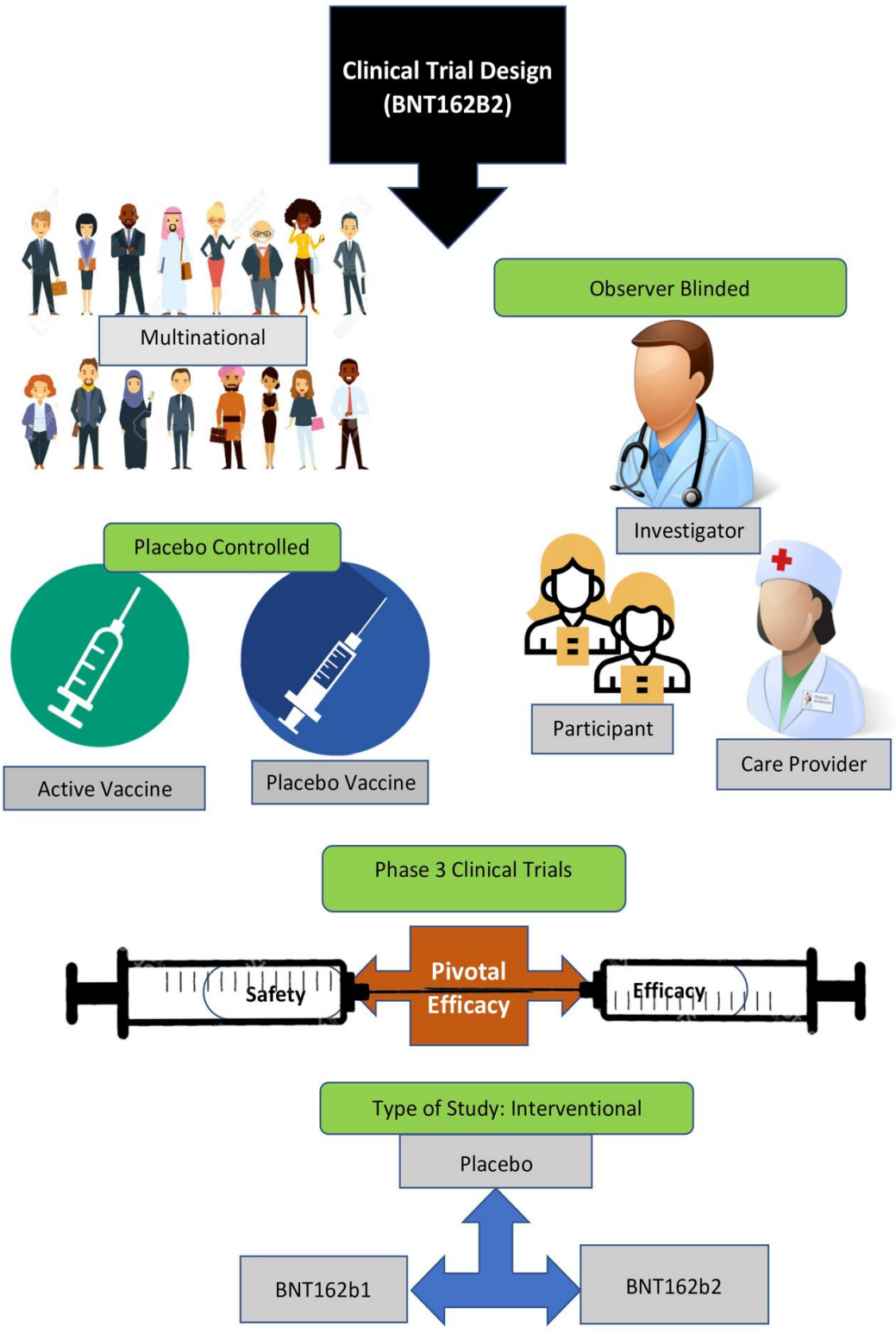
- The pfizer-BionTech Covid-19 vaccine has not been approved or licensed by the U.S.FDA but has been authorized for emergency use by FDA, under an Emergency Use Authorization (EUA) to prevent coronavirus.
- (COVID-19) for use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of this product unless the declaration is terminated or authorization revoked sooner.

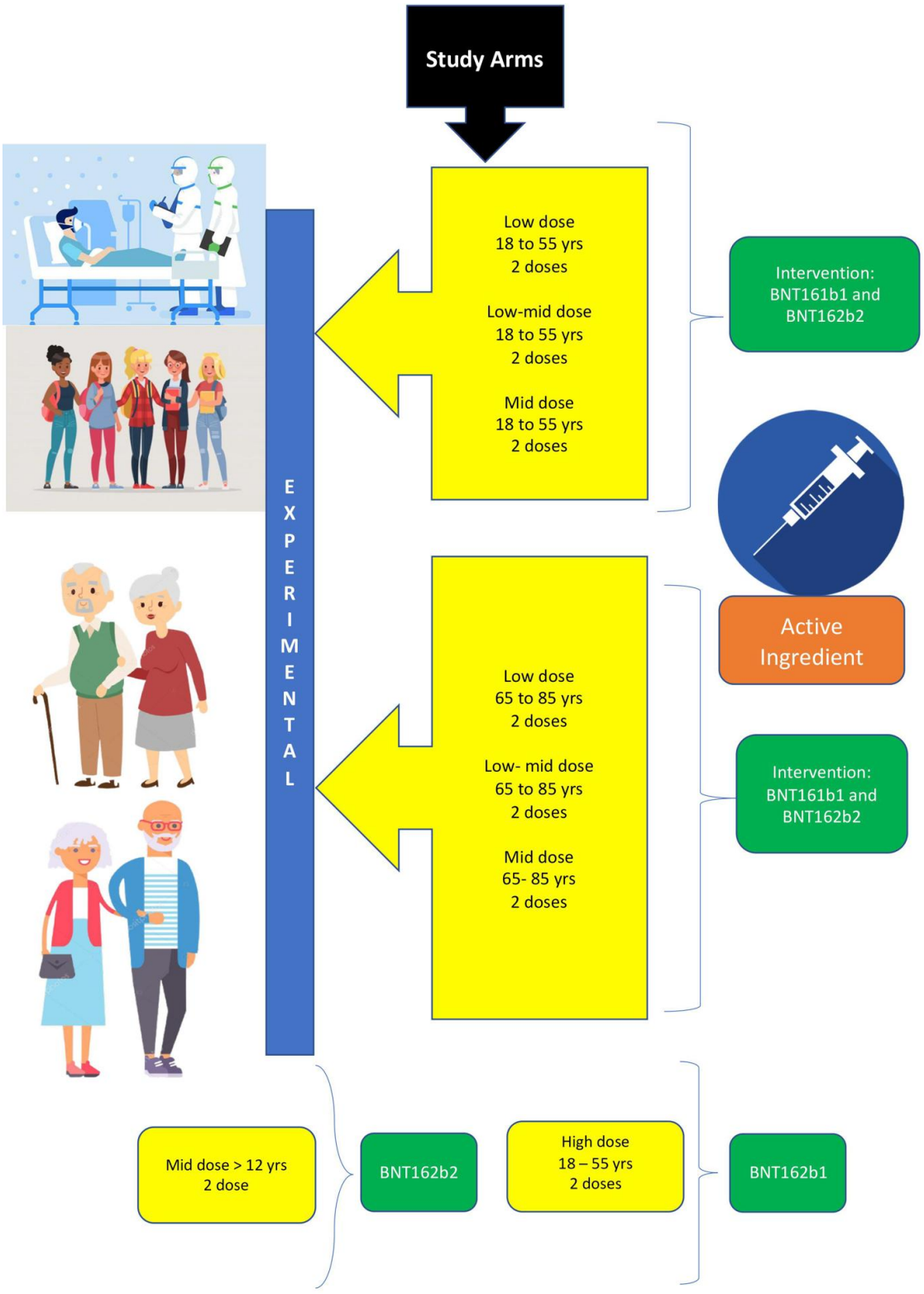

Mechanisms Of Action of Pfizer-BNT162b2
Healthy Volunteer
COVID-19 Patient
MECHANISM
VACCINE
Pfizer- BNT162b2 vaccine
AUGAUCUCGUAA
mRNA
Contains Genetic Instructions
Met
Ile
Ser
STOP
Polypeptide
Spike protein
Build coronavirus protein called 'Spike' protein
VACCINE
Human cells
Spike protein
When Injected into cells this vaccine causes them to make spike protein
IMMUNITY
Then released into the body produce an immune response

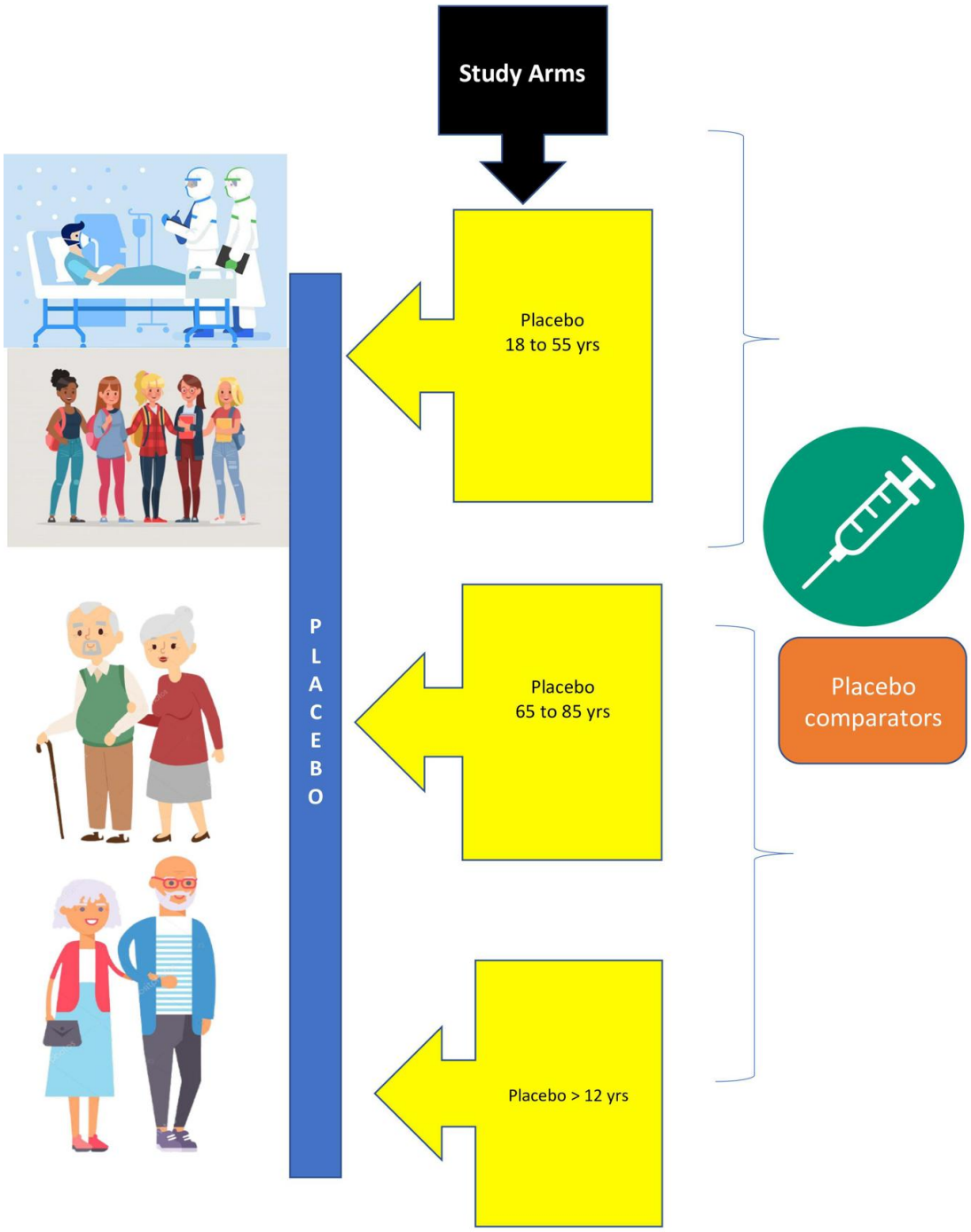
Sr.no	Inclusion Criteria	Exclusion Criteria
1	Male and Female participants of age 18 to 55 yrs can enrol for the study.	History of anaphylaxis are not included in the study.
2	Participants who can follow schedule visits, study procedures.	Phase 1 only: those who have medical conditions/ pre-existing conditions like hypertension, obesity, asthma.
3	Who is educated and can sign Informed consent form before the study.	Pregnant and Breastfeeding women's are not included in the study.
4	Healthy participants are included in the phase 1 study.	

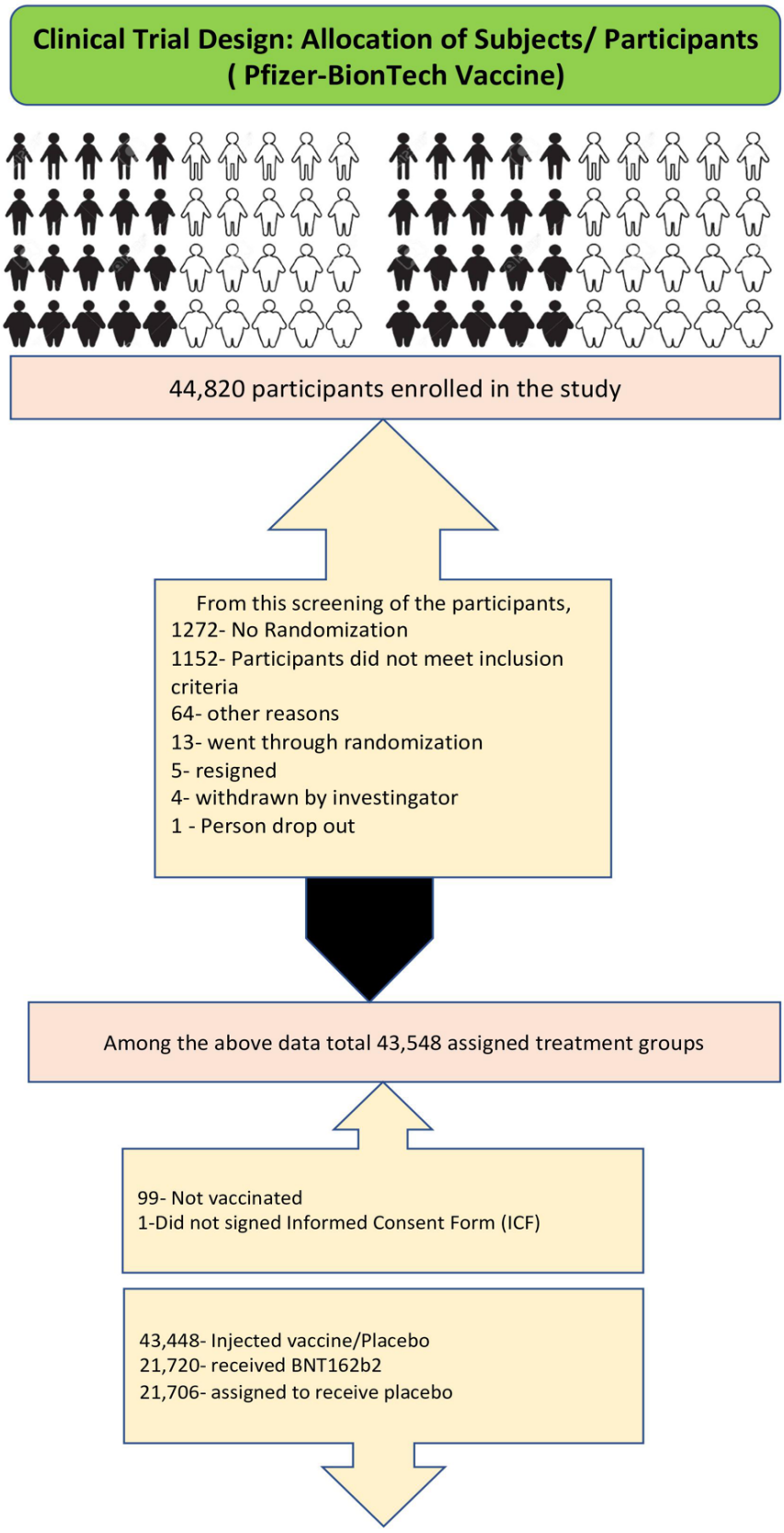
Pfizer: BNT162B2 Ensuring Patient Safety during the study

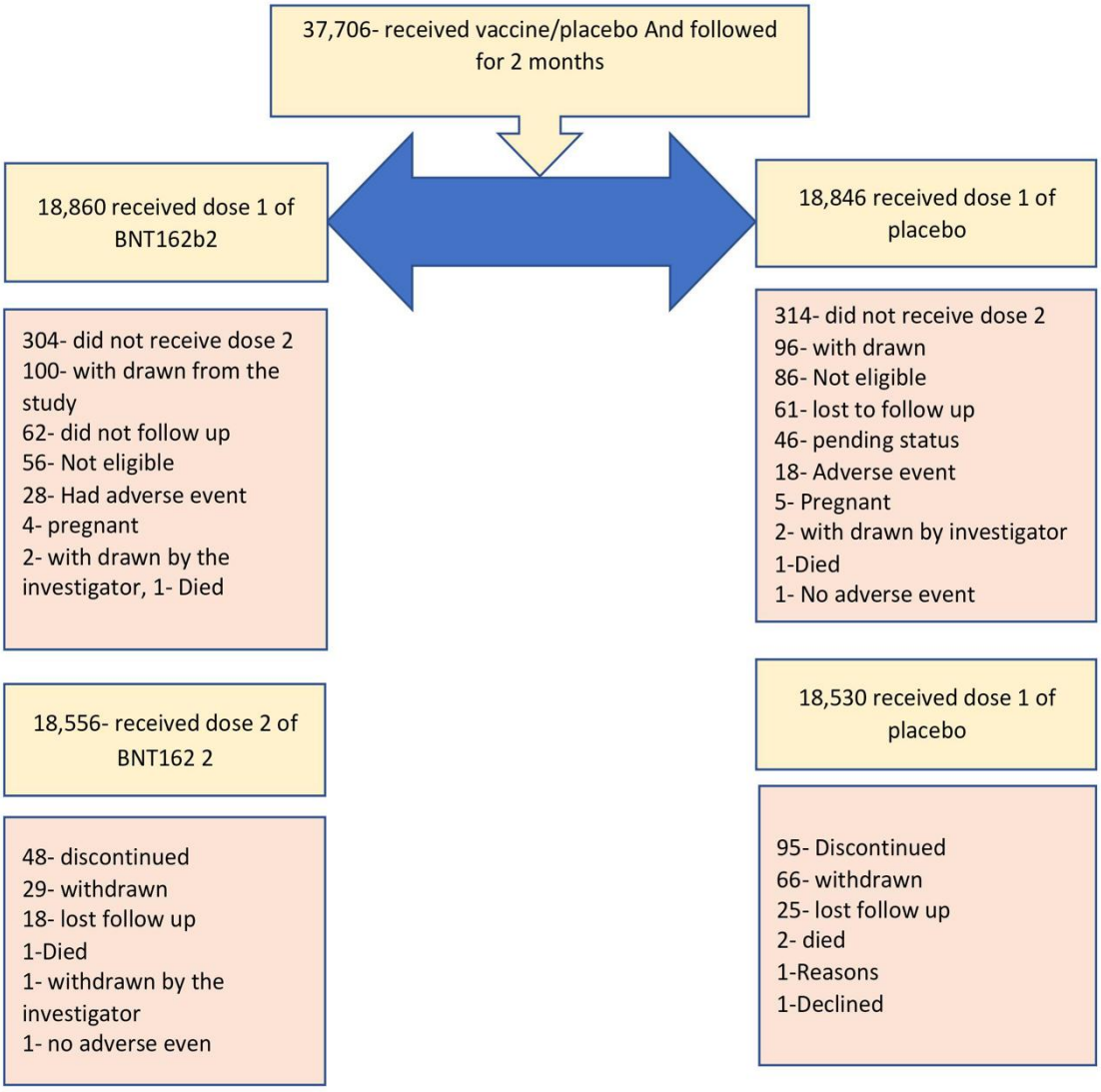



Clinical Trial Design (BNT162B2)
Multinational
Observer Blinded
Investigator
Placebo Controlled
Active Vaccine
Placebo Vaccine
Participant
Care Provider
Phase 3 Clinical Trials
Safety
Pivotal Efficacy
Efficacy
Type of Study: Interventional
Placebo
BNT162b1
BNT162b2


Study Arms
Low dose
18 to 55 yrs
2 doses
Low-mid dose
18 to 55 yrs
2 doses
Mid dose
18 to 55 yrs
2 doses
Intervention:
BNT161b1 and
BNT162b2
EXPERIMENTAL
Active
Ingredient
Low dose
65 to 85 yrs
2 doses
Low- mid dose
65 to 85 yrs
2 doses
Mid dose
65- 85 yrs
2 doses
Intervention:
BNT161b1 and
BNT162b2
Mid dose > 12 yrs
2 dose
BNT162b2
High dose
18 – 55 yrs
2 doses
BNT162b1


Study Arms
Placebo
18 to 55 yrs
PLACEBO
Placebo
65 to 85 yrs
Placebo > 12 yrs
Placebo
comparators

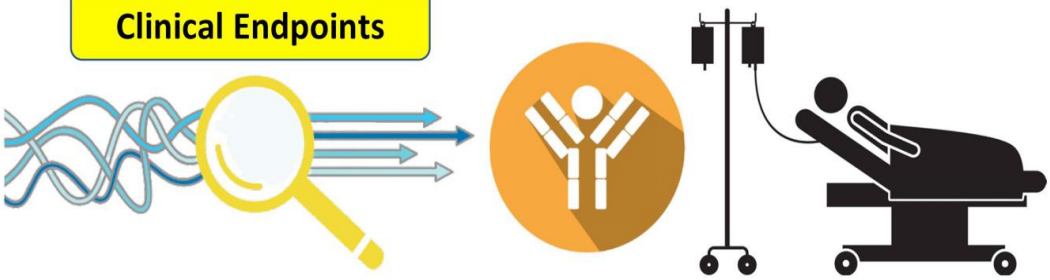

Clinical Trial Design: Allocation of Subjects/ Participants
(Pfizer-BionTech Vaccine)
44,820 participants enrolled in the study
From this screening of the participants,
1272- No Randomization
1152- Participants did not meet inclusion criteria
64- other reasons
13- went through randomization
5- resigned
4- withdrawn by investingator
1 - Person drop out
Among the above data total 43,548 assigned treatment groups
99- Not vaccinated
1-Did not signed Informed Consent Form (ICF)
43,448- Injected vaccine/Placebo
21,720- received BNT162b2
21,706- assigned to receive placebo


37,706- received vaccine/placebo And followed for 2 months
18,860 received dose 1 of BNT162b2
18,846 received dose 1 of placebo
304- did not receive dose 2
100- with drawn from the study
62- did not follow up
56- Not eligible
28- Had adverse event
4- pregnant
2- with drawn by the investigator, 1- Died
314- did not receive dose 2
96- with drawn
86- Not eligible
61- lost to follow up
46- pending status
18- Adverse event
5- Pregnant
2- with drawn by investigator
1-Died
1- No adverse event
18,556- received dose 2 of BNT162 2
18,530 received dose 1 of placebo
48- discontinued
29- withdrawn
18- lost follow up
1-Died
1- withdrawn by the investigator
1- no adverse even
95- Discontinued
66- withdrawn
25- lost follow up
2- died
1-Reasons
1-Declined

Primary Efficacy Endpoints:
First Primary endpoint:
COVID-19 incidence per 1000 person-years of follow-up in participants without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥7 days after Dose 2

Second primary endpoint:
COVID-19 incidence per 1000 person-years of follow-up in participants with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥7 days after Dose 2

Clinical Endpoints

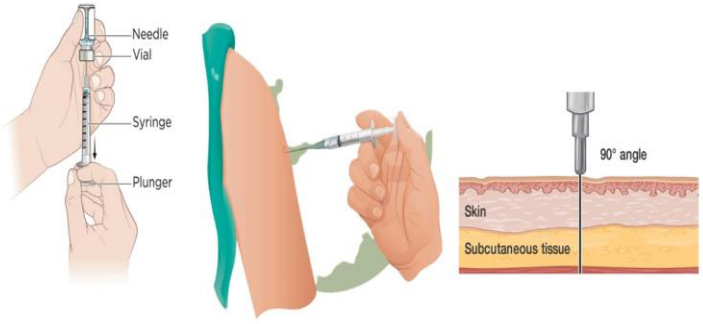


Secondary Efficacy Endpoints:
COVID-19 confirmed at least 14 days after Dose 2: COVID-19 incidence per 1000 person- years of follow up in participants either (1) without or (2) with and without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥14 days after Dose 2

2Severe COVID-19: incidence per 1000 person-years of follow-up in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed either (1) ≥7 days after Dose 2 or (2) ≥14 days after Dose 2

CDC-defined COVID-19: incidence per 1000 person-years of follow-up in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed either (1) ≥7 days after Dose 2 or (2) ≥14 days after Dose 2

Route Of Administration: Intramuscular injection

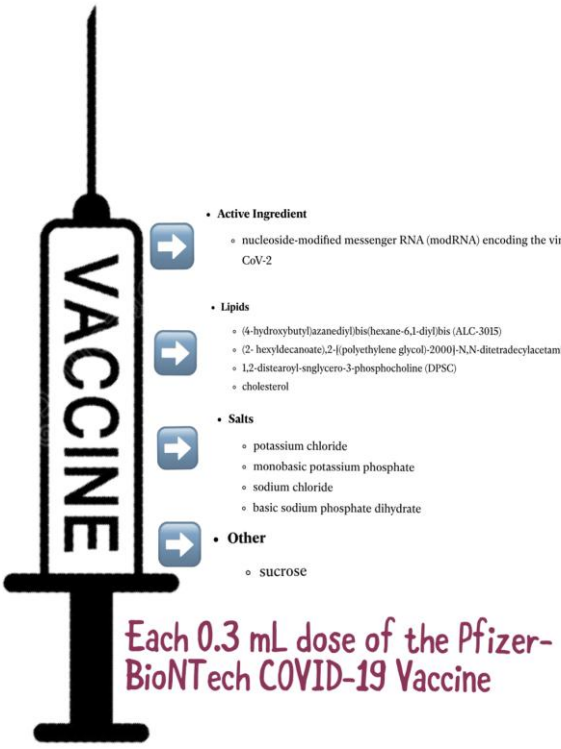


Pfizer-BioNTech COVID-19 Vaccine vaccination series is 2 doses

1st Dose

2nd Dose

Given 3 weeks apart.



- **Active Ingredient**
  - nucleoside-modified messenger RNA (modRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2
- **Lipids**
  - (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis (ALC-3015)
  - (2- hexyldecanoate),2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
  - 1,2-distearoyl-snglycero-3-phosphocholine (DPSC)
  - cholesterol
- **Salts**
  - potassium chloride
  - monobasic potassium phosphate
  - sodium chloride
  - basic sodium phosphate dihydrate
- **Other**
  - sucrose

Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine

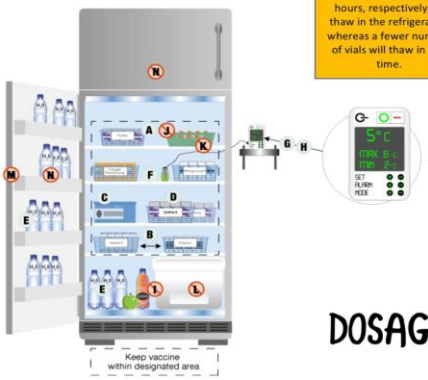
Storage and Handling:
During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Do not refreeze thawed vials.

The thermal container maintains a temperature range of -90oC to -60oC (-130oF to -76oF). Storage within this temperature range is not considered an excursion from the recommended storage condition.

Thawed Vials Before Dilution
Thawed Under Refrigeration
Thaw and then store undiluted vials in the refrigerator [2oC to 8oC (35oF to 46oF)] for up to 5 days (120 hours). A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

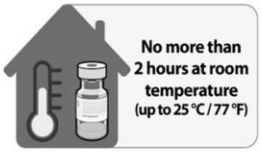
Vials After Dilution
- After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution.
- During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.
- Any vaccine remaining in vials must be discarded after 6 hours.
- Do not refreeze.

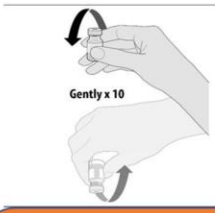
Thawed at Room Temperature
For immediate use, thaw undiluted vials at room temperature [up to 25oC (77oF)] for 30 minutes. Thawed vials can be handled in room light conditions. Vials must reach room temperature before dilution.
Undiluted vials may be stored at room temperature for no more than 2 hours.



DOSAGE AND ADMINISTRATION

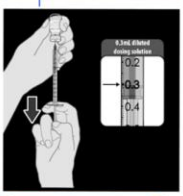
THAWING PRIOR TO DILUTION





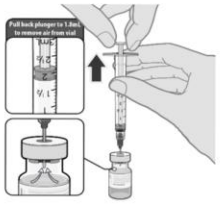
- Do not shake.
- Inspect the liquid in the vial prior to dilution.
- The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discoloured or if other particles

DILUTION



- Obtain sterile 0.9% Sodium Chloride Injection.
- Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
- Cleanse the vaccine vial stopper with a single-use antiseptic swab
- Add 1.8 mL of 0.9% Sodium Chloride

EQUALIZE



Equalise vial pressure before removing the needle from the vial by withdrawing 1.8 mL of air into the empty diluent syringe

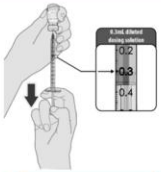
INVERT

Gently invert the vial containing the Pfizer COVID-19 Vaccine 10 times to mix

RECORD AND STORE

- Record the date and time of dilution on the Pfizer-BioTech COVID- 19 Vaccine vial label
- Store between 2°C to 25°C (35°F to 77°F)
- Discard any unused vaccine 6 hours after dilution

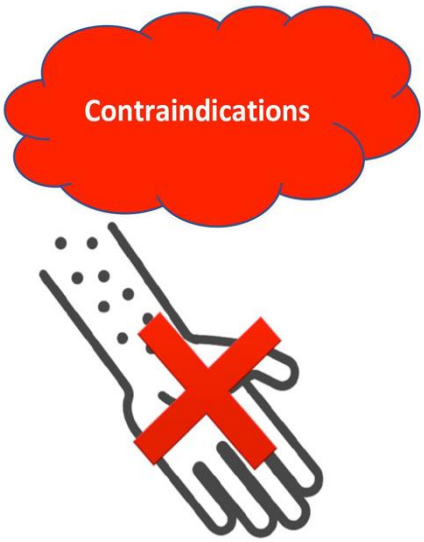
CLEANSE



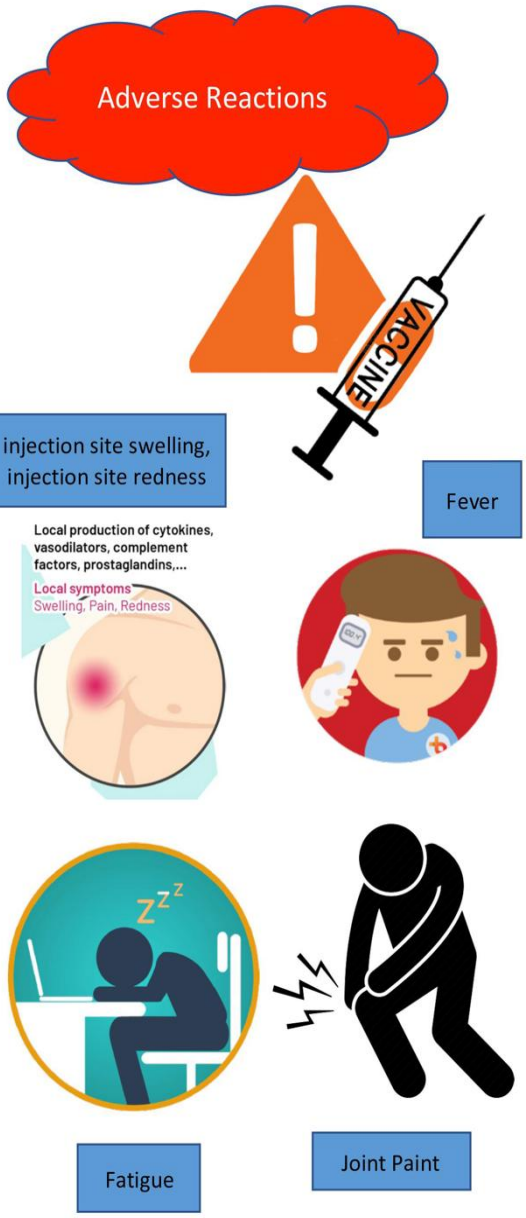
- Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of the Pfizer COVID-19 Vaccine
- Administer immediately

Dilution and dose preparation instructions


Pregnancy
All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognised pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on Pfizer COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.
Geriatric Use
Clinical studies of Pfizer COVID-19 Vaccine include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy. total number of Pfizer COVID-19 Vaccine recipients in Study 2 (N=20,033), 21.4% (n=4,294) were 65 years of age and older and 4.3% (n=860) were 75 years of age and older.
USE IN SPECIFIC POPULATIONS
Lactation
Data are not available to assess the effects of Pfizer COVID-19 Vaccine on the breastfed infant or on milk production/excretion.
Paediatric Use
Emergency Use Authorisation of Pfizer COVID-19 Vaccine in adolescents 16 and 17 years of age is based on extrapolation of safety and effectiveness from adults 18 years of age and older. Emergency Use Authorisation of Pfizer COVID-19 Vaccine does not include use in individuals younger than 16 years of age.



Do not administer Pfizer COVID-19 Vaccine to individuals with known history of a severe allergic reaction (e.g., anaphylaxis)

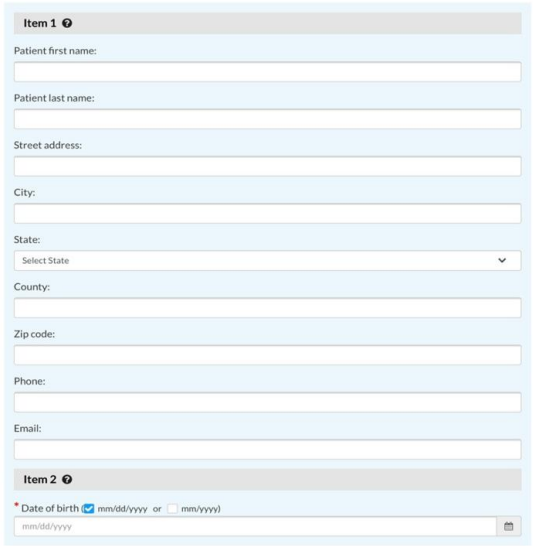


Reporting Adverse Events: individuals can send the reports of their experience, Any adverse event that occurs after the administration of a vaccine.
Link: https://vaers.hhs.gov/reportevent.html

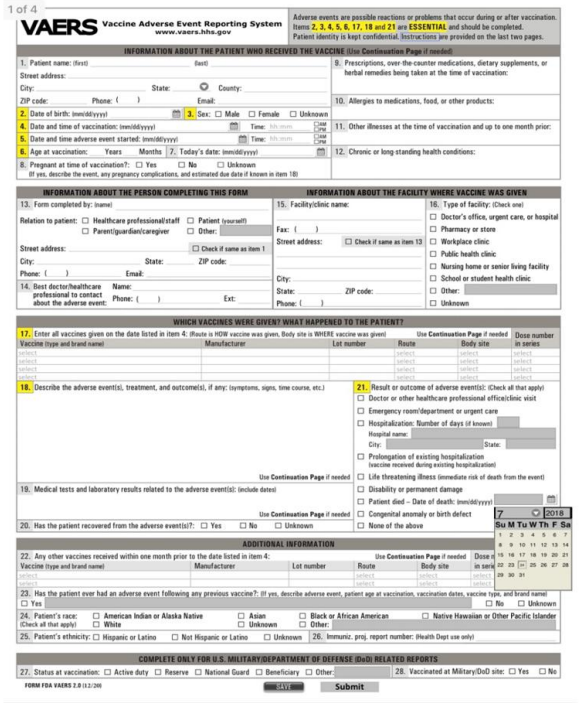
VAERS Vaccine Adverse Event Reporting System
www.vaers.hhs.gov

There are 3 ways to report adverse events.

Report online to VAERS:



Report using a writable PDF form



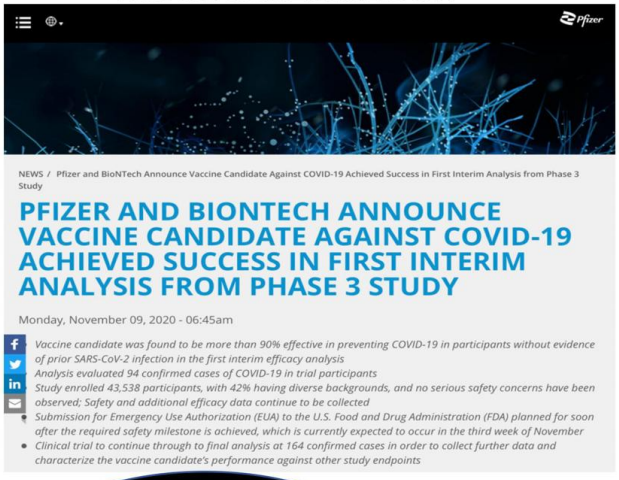
If you need further assistance with reporting to VAERS, please email info@VAERS.org or call 1-800-822-7967.


you can report side effects:
HTTP
https://www.pfizersafetyreporting.com/#/en
FAX
1-866-635-8337
1-800-438-1985


A growing number of countries have also given emergency authorization for Comirnaty.
Canada
U.S.
Britain and the E.U
Switzerland
Panama
Kuwait
Bahrain
Saudi Arabia
Mexico
Argentina
Costa Rica
Ecuador

Sources of Official Information

DOI: 10.1056/NEJMoa2034577

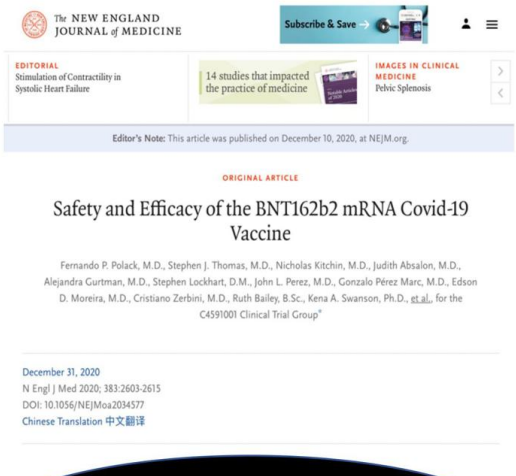


NEWS / Pfizer and BioNTech Announce Vaccine Candidate Against COVID-19 Achieved Success in First Interim Analysis from Phase 3 Study

PFIZER AND BIONTECH ANNOUNCE VACCINE CANDIDATE AGAINST COVID-19 ACHIEVED SUCCESS IN FIRST INTERIM ANALYSIS FROM PHASE 3 STUDY

Monday, November 09, 2020 - 06:45am

- *Vaccine candidate was found to be more than 90% effective in preventing COVID-19 in participants without evidence of prior SARS-CoV-2 infection in the first interim efficacy analysis*
- *Analysis evaluated 94 confirmed cases of COVID-19 in trial participants*
- *Study enrolled 43,538 participants, with 42% having diverse backgrounds, and no serious safety concerns have been observed; Safety and additional efficacy data continue to be collected*
- *Submission for Emergency Use Authorization (EUA) to the U.S. Food and Drug Administration (FDA) planned for soon after the required safety milestone is achieved, which is currently expected to occur in the third week of November*
- *Clinical trial to continue through to final analysis at 164 confirmed cases in order to collect further data and characterize the vaccine candidate's performance against other study endpoints*



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Editor's Note: This article was published on December 10, 2020, at NEJM.org.

ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Fernando P. Polack, M.D., Stephen J. Thomas, M.D., Nicholas Kitchin, M.D., Judith Absalon, M.D., Alejandra Gurtman, M.D., Stephen Lockhart, D.M., John L. Perez, M.D., Gonzalo Pérez Marc, M.D., Edson D. Moreira, M.D., Cristiano Zerbini, M.D., Ruth Bailey, B.Sc., Kena A. Swanson, Ph.D., et al., for the C4591001 Clinical Trial Group*

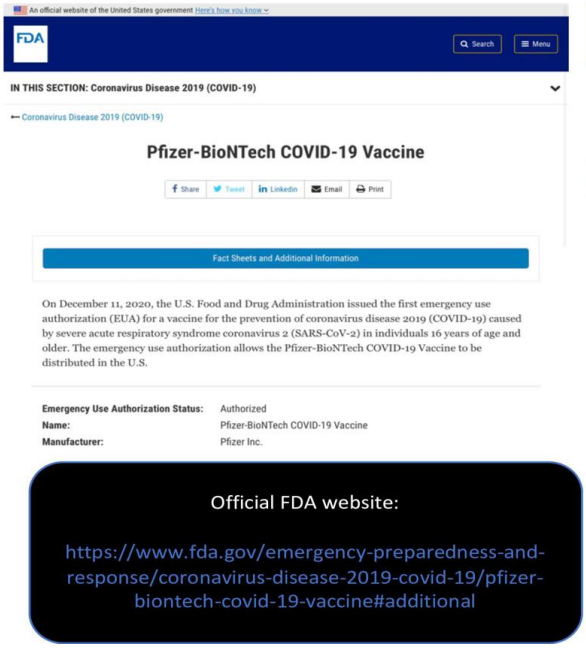
December 31, 2020
N Engl J Med 2020; 383:2603-2615
DOI: 10.1056/NEJMoa2034577
Chinese Translation 中文翻译

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-vaccine-candidate-against

Pfizer official website

DOI:10.1056/NEJMoa2034577

Published in: The New England of Medicine



An official website of the United States government

FDA

Search | Menu

IN THIS SECTION: Coronavirus Disease 2019 (COVID-19)

← Coronavirus Disease 2019 (COVID-19)

Pfizer-BioNTech COVID-19 Vaccine

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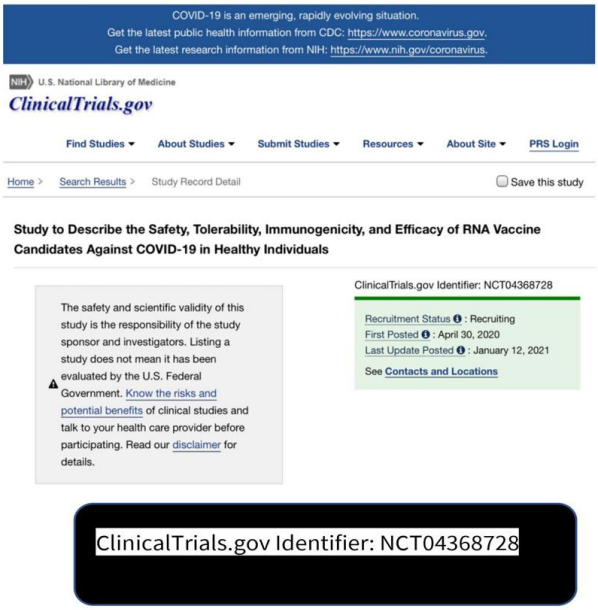
Fact Sheets and Additional Information

On December 11, 2020, the U.S. Food and Drug Administration issued the first emergency use authorization (EUA) for a vaccine for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. The emergency use authorization allows the Pfizer-BioNTech COVID-19 Vaccine to be distributed in the U.S.

Emergency Use Authorization Status:	Authorized
Name:	Pfizer-BioNTech COVID-19 Vaccine
Manufacturer:	Pfizer Inc.

Official FDA website:

https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine#additional



COVID-19 is an emerging, rapidly evolving situation.
Get the latest public health information from CDC: https://www.coronavirus.gov.
Get the latest research information from NIH: https://www.nih.gov/coronavirus.

U.S. National Library of Medicine

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Study to Describe the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

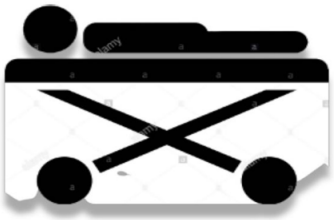
ClinicalTrials.gov Identifier: NCT04368728

Recruitment Status : Recruiting
First Posted : April 30, 2020
Last Update Posted : January 12, 2021

See Contacts and Locations

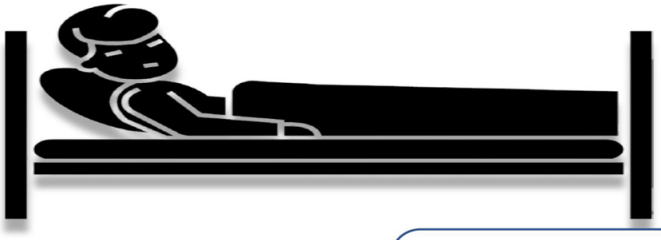
ClinicalTrials.gov Identifier: NCT04368728

Recent Study



Recent Study Published in thebmj journal:
In Norway doctors are recommended to find why the health triggered of these patients and determined whether are there any side effects? of these vaccinations but according to the reports after vaccination side effects may led life threatening conditions in some patients.
Pharmacovigilance: 33 were suspected adverse drug reactions, age group of the patient over 75.

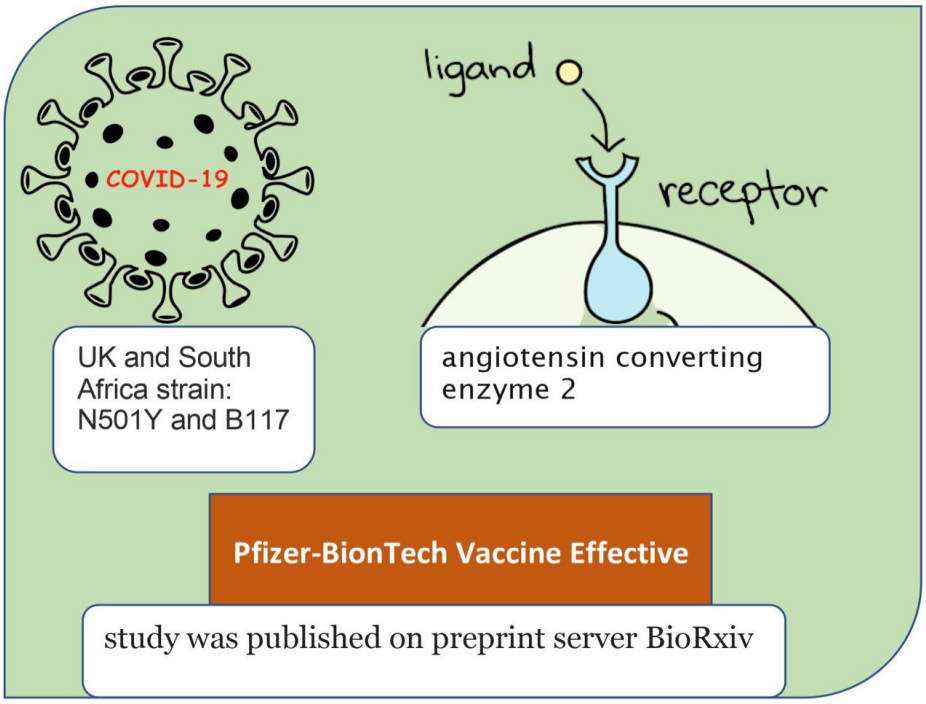
Clinical Frailty Scale:



8 Very severely frail conditions: End of life

8 Terminally ill: Life expectancy less than 6 months

Conclusion:
Comparison between (A) observed death rate in older vaccine subjects > (B) expected death rate in frailty and morbidity.



II. CONCLUSION:

1) This pictorial data will build confidence in the global health opportunity for vaccines to help combat this devastating pandemics.
2) This pictorial representation helps to understand in the easy way and highlights the points in focus.
3) This pictorial representation provides the overview of pfizer-BionTech vaccine from lab to clinical trial designing and understanding the basic concepts.
4) From the clinical trial data how we can represent is shown in this article.
5) It may help health care industry to represent data in a pictorial representation format.
6) Time consuming
7) Organising all data in to one pictorial information is the easy way to understand the clinical trial designs.

REFERENCES:

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[2]. https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine
[3]. Fernando P. Polack, M.D,Stephen J. Thomas, M.D,Nicholas Kitchin et.al, " Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine", N Engl J Med 2020; 383:2603-2615, DOI: 10.1056/NEJMoa2034577
[4]. https://www.who.int/news-room/feature-stories/detail/who-can-take-the-pfizer-biontech-covid-19--vaccine
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