**LAPORAN PENELITIAN**

**Judul Penelitian :**

# CAUSALITY ASSESSMENT OF ADVERSE EVENT FOR COVID-19 VACCINE IN COMPARISON BETWEEN RACIAL CLASSIFICATION USING NARANJO ALGORITHM


**Oleh :**

**apt. Rachma Dessidianti, S.Farm, M.Sc**

**Nabila Mirza Azizi (20201666030)**

**Malika Ilma Alkautsar (20201666017)**



**FAKULTAS ILMU KESEHATAN**

**UNIVERSITAS MUHAMMADIYAH SURABAYA**

Jl. Sutorejo No. 59 Surabaya 60113

Telp. 031-3811966

http://www.um-surabaya.ac.id

**HALAMAN PENGESAHAN**

| | | |
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| Skema | : | |
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| Ketua Peneliti | | |
| a. Nama Lengkap | : | Apt. Rachma Dessidianti, S.Farm, M.Sc |
| b. NIDN | : | - |
| c. Jabatan Fungsional | : | - |
| d. Program Studi | : | S1 Farmasi |
| e. No Hp | : | 08123046196 |
| f. Alamat Email | : | racmadessidianti@um-surabaya.ac.id |
| Anggota Mahasiswa (1) | | |
| a. Nama Lengkap | : | Malika Ilma Alkautsar |
| b. NIM | : | 20201666017 |
| c. Perguruan Tinggi | : | Universitas Muhammadiyah Surabaya |
| Anggota Mahasiswa (2) | | |
| a. Nama Lengkap | : | Nabila Mirza Azizi |
| b. NIM | : | 20201666030 |
| c. Perguruan Tinggi | : | Universitas Muhammadiyah Surabaya |

Mengetahui,
Dekan FIK UMSurabaya

Dr. Nur Mukarromah, SKM.,M.Kes
NIDN. 0713067202

Surabaya, 12 April 2022
Ketua Peneliti

Rachma Dessidianti, S.Farm, M.Sc

Menyetujui
Ketua LPPM UMSurabaya

Dede Nasrullah, S.Kep., Ns., M.Kep
NIDN. 0730016501

# Causality Assessment of Adverse Events for Covid-19 Vaccine in Comparison Between Racial Classification Using Naranjo Algorithm

Rachma Dessidianti(✉), Fuad Muzakky, and Karima Samlan

University of Muhammadiyah Surabaya, Surabaya, Indonesia
rachmadessidianti@gmail.com

**Abstract.** In pharmacovigilance, causality assessment remains an important approach to analyze the causal relationship between adverse events and vaccine application. In 2020, the rapid development of COVID-19 vaccines became a global imperative. Vaccine development typically takes decades before it is approved. However, due to the severityof the pandemic, clinical trials have been cut short.

Objective: The Naranjo algorithm was used to compare the causality assessment of adverse events for the COVID-19 vaccine across racial classifications.

Methods: This was a descriptive type of quantitative observational research. Naranjo algorithm was used as a probability scale to standardize causality assessments for adverse events. Respondent data were obtained in the form of numbers which will then be classified.

Results: For each racial classification, the majority of the causality assessments of adverse events following COVID-19 vaccination were in the "Probable" (30.0%) and "Possible" (41.4%) groups. In the "Probable" group, the percentage of the Caucasian race is 42.1%, Asian is 29.7%, Black/African is 33.3%, and another race is 9.1%. While in the "Possible" group, the Caucasian, Asian, Black/African and other races were 31.6%, 37.8%, 66.7%, and 63.6%, respectively.

Conclusion: The "Probable" category includes adverse events that (1) had a reasonable time-related continuity after vaccine application, (2) had a recognized response to the suspected vaccine, (3) were confirmed by withdrawal but not by exposure to the vaccine application, and (4) could not be reasonably exposed by known clinical characteristics of the patient. The "possible" group indicates that the adverse events (1) had a time-related continuity after vaccine application, (2) possibly exhibited a recognized pattern to the suspected vaccine, and (3) could be explained by the patient's disease characteristics.

**Keywords:** Adverse events · Causality assessment · Naranjo algorithm

## 1 Introduction

In pharmacovigilance, causality assessment remains an important approach to analyze the causal relationship between adverse events (side effects) and vaccine application [1]. To assess the causal relationship between vaccine application and adverse events,


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three types of causality assessment methods are available: algorithm-based approaches, expert judgment or global introspection, and probabilistic or Bayesian approaches [2]. There is no single method that is accepted as the best standard for analyzing causality assessment, as evidenced by the various available methods, and each method has its own advantages and limitations [3, 4].

Naranjo is an algorithm-based causality assessment method that has been widely used [3–5]. The Naranjo algorithm was created to track adverse events in clinical trials. However, in its development, the Naranjo Algorithm is also used by health professionals to assess adverse events. On the other hand, the pharmaceutical industry also frequently uses this method for processing initial cases, which are then reported as final conclusions in binary terms such as 'Related' or 'Unrelated' when presenting the results to regulatory authorities [6–8]. The Naranjo algorithm includes a short and simple method for separating scores for each point, which reduces intra- and inter-observer variation and has good reproducibility [3, 4, 9]. The advantage of the Naranjo algorithm is by providing scores for aspects such as temporality, alternative explanations, and responses to additional questions [3, 10].

The novel coronavirus 2019 (2019-nCoV), also known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spread quickly from its origin in Wuhan, Hubei Province, China, to the rest of the world [11]. On October 7, 2022, WHO reported 617,597,680 confirmed cases of COVID-19, including 6,532,705 deaths. The vaccine had been administered a total of 12,723,216,322 times as of October 3, 2022 [12]. According to WHO, there were 6,442,624 confirmed cases of COVID-19 in Indonesia from January 3, 2020 to October 7, 2022, with 158,192 deaths. A total of 438,360,363 doses of vaccine had been administered as of October 1, 2022 [12].

Rapid vaccine development for the COVID-19 is becoming a global imperative. A global pandemic would result in high mortality, severe economic disruption, and major changes in people's lives. The advantages of developing an effective vaccine include the ability to prevent a repeat or ongoing pandemic in a timely manner [13].

Vaccine development is typically measured in decades, from the time we have access to an approved vaccine until it is ready for widespread distribution. However, in the case of the COVID-19 pandemic, all stakeholders are attempting to research and develop a COVID-19 vaccine as soon as possible, ideally before the end of 2020 or early 2021. Clinical trials have been shortened due to the severity of the pandemic. This is unprecedented. New manufacturing platforms, structure-based antigen design, computational biology, protein engineering, and gene synthesis, on the other hand, have given us the tools we need to produce vaccines quickly and precisely [13].

Antiviral vaccines are divided into two categories. The first type of vaccine is gene-based, which provides a sequence of genes encoding protein antigens produced by the host cell. Live virus vaccines, recombinant vaccine vectors, and nucleic acid vaccines are examples of these. Protein-based vaccines, which are generated in vitro, include inactivated viruses as a whole, individual viral proteins or subdomains, or viral proteins constructed as particles. Recombinant vaccine vectors and nucleic acid vaccines are thought to be ideal for mass production because they are easier to integrate into platform manufacturing technologies, which have the same upstream supply chain and

downstream processes for each product. Accuracy is achieved by recognizing the atomic structure of the vaccine antigen and protecting the target epitope [13].

The most effective treatment for COVID-19 cases, as well as a community-wide vaccine, is critical. Aside from a vaccine, there is no specific drug to treat COVID-19 worldwide. Many countries use COVID-19 vaccines of various types, including BNT162b2 (Pfizer) messenger RNA (mRNA) vaccine, mRNA-1273 vaccine (Moderna), ChAdOx1 nCoV-19/AZD1222 vaccine (AstraZeneca), Sinovac, and Sinopharm vaccines. To demonstrate the coronavirus spike protein, AstraZeneca Oxford vaccines, Johnson & Johnson, and Sputnik engineered live virus vectors, whereas vaccines developed by Pfizer and Moderna use cutting-edge technology such as messenger RNA [14, 15]. The Sinopharm vaccine consists of an inactivated COVID-19 antigen [16].

Based on World Health Organization, COVID-19 vaccination started in late December 2020, while on January 13, 2021, the first phase of vaccination began in Indonesia [17]. The availability of more than one type of vaccine creates challenges for monitoring adverse events. The manufacture of various COVID-19 vaccines uses different viral strains so that it can be predicted that it will lead to the emergence of several types of adverse events [18].

## 2 AIM

This study aimed to compare the causality assessment of adverse events for the COVID-19 vaccine using the Naranjo algorithm and the shortened clinical trial process.

## 3 Method

### 3.1 Research Design

This was a descriptive type of quantitative observational research describing the research object. Respondent data was collected in the form of numbers, which were then classified in order to describe the results [19].

The Adverse Events Probability Scale, also known as the Naranjo scale, was developed in 1991 by Naranjo of the University of Toronto. This scale was created to standardize the assessment of causality for all adverse vaccine events. This scale is also intended for randomized controlled trials, vaccine registration studies, and routine clinical practice. Naranjo's algorithm is easy to use and widely used [19].

There are ten questions on the Naranjo probability scale with the answers "Yes," "No," or "Do Not Know". Each answer receives a different point value (−1, 0, +1, or +2). The following is a condensed version of the ten questions [20] (Table 1):

**Table 1.** Naranjo Algorithm, also known as the Naranjo Probability Scale

| No. | Question | Yes | No | Do Not Know |
|---|---|---|---|---|
| 1. | Was there any prior documented reports of unfavorable reactions (side effects) to the COVID-19 vaccine? | +1 | 0 | 0 |
| 2. | Did the adverse event (side effect) following vaccination appear after the vaccine was injected? | + 2 | −1 | 0 |
| 3. | Did the adverse event (side effect) following vaccination improve when the vaccine was withdrawn, or a specific antagonist was used? | +1 | 0 | 0 |
| 4. | Are there any other possible causes (other than the vaccine) that could have caused the reaction? | −1 | +2 | 0 |
| 5. | When the vaccine was re-administered, did the reaction return? | +2 | −1 | 0 |
| 6. | Did the reaction reappear after the placebo was administered? | −1 | +1 | 0 |
| 7. | Was the vaccine found in blood (or other bodily fluids) at toxic concentrations? | +1 | 0 | 0 |
| 8. | Did the adverse event (side effect) brought on by the vaccination get worse as the dose was increased? Or did the unpleasant event (side effect) that followed the vaccination get milder as the dose was reduced? | +1 | 0 | 0 |
| 9. | Did you have a similar adverse event (side effect) following vaccination to the same or similar vaccine in any previous exposure? | +1 | 0 | 0 |
| 10. | Was there any verifiable evidence to support the adverse event (side effect) following the vaccination? | +1 | 0 | 0 |

### 3.2 Study Participants

The sample used in this study was the citizen in Indonesia and Hungary with racial classification who have been vaccinated against COVID-19, with a number of samples of 70 respondents.

### 3.3 Instrument and Data Collection

The data collection techniques and instruments used in this study were questionnaires using the Naranjo algorithm, which was used to determine the possibility of the adverse event being caused by vaccines rather than other factors. The questionnaire itself was a data measurement tool in the form of statements submitted to the respondent.

The research instrument consisted of sociodemographic questions (age, occupation, gender, and education) and questions related to adverse events following the COVID-19 vaccination of respondents. This survey was distributed to respondents, and data was collected using Google Form [19].

**Table 2.** Scores Interpretation of Naranjo Algorithm

| Score | Score Interpretation |
|---|---|
| Total score $\geq 9$ | **Definite**. The reaction (1) demonstrated a reasonable temporal sequence following a vaccine or in which a toxic vaccine level had been established in body fluids or tissues, (2) demonstrated a recognized response to the suspected vaccine, and (3) was confirmed by improvement after withdrawal of the vaccine and reappearance after the reexposure |
| Total Score 5 to 8 | **Probable**. The reaction (1) demonstrated reasonable time-related continuity after vaccine application, (2) demonstrated a recognized response to the suspected vaccine, (3) was confirmed by withdrawal but not by exposure to the vaccine application, and (4) could not be reasonably explained by known clinical characteristics of the patient |
| Total Score 1 to 4 | **Possible**. The reaction (1) demonstrated time-related continuity following vaccine application, (2) possibly exhibited a recognized pattern to the suspected vaccine, and (3) could be explained by the patient's disease characteristics |
| Total Score $\leq 0$ | **Doubtful**. The reaction was most likely caused by something other than the vaccine |

### 3.4 Data Analysis of Causality Assessment Interpretation Scores

By responding "Yes," "No," or "Do Not Know" to ten questions about the temporal sequence, dechallenge, rechallenge, alternative causes, placebo response, vaccine levels in body fluids or tissues, dose-response relationship, history of prior adverse events, and confirmation with other sources, the Naranjo algorithm [10] was used to assess the causal relationship between an identified undesirable clinical adverse event and vaccine [20]. The process yielded a final score ranging from $-4$ to $+13$, allowing vaccine causality to be classified into four categories: "Definite" (score 9), "Probable" (score between 5 and 8), "Possible" (score between 1 and 4), and "Doubtful" (score 0) [1] (Table 2).

## 4 Results and Discussion

### 4.1 Patients Demography

The samples obtained from the results of the questionnaire were 70 respondents who received the COVID-19 vaccine. There were 53 female respondents, with a percentage of 76%, and 17 male respondents, with a percentage of 24%. The age group 21–30 years received the most responses, with a total of 38 (54%), followed by the age group 31–40 years, with a total of 26 (37%) (Table 3).

The racial of respondents were classified into four groups, namely Caucasian/White, Asian, Black, or African American and Other Race. The number of Caucasian/White respondents was 19, with a percentage of 27.1%. Asian respondents were 37 (52.9%), Black or African American respondents were 3 (4.3%), while other races amounted to 11 people with a percentage of 15.7%.

**Table 3.** Demographic Characteristics

| No. | Demographic Characteristics | Number of respondents | Percentage |
|---|---|---|---|
| 1 | **Sex** | | |
| | Male | 17 | 24% |
| | Female | 53 | 76% |
| | Total | 70 | 100% |
| 2. | **Race and Ethnicity** | | |
| | Caucasian / White | 19 | 27.1% |
| | Asian | 37 | 52.9% |
| | Black or African American | 3 | 4.3% |
| | Other Race | 11 | 15.7% |
| | Total | 70 | 100.0% |
| 3. | **Age** | | |
| | 21–30 years old | 38 | 54% |
| | 31–40 years old | 26 | 37% |
| | 41–50 years old | 4 | 6% |
| | 51–60 years old | 2 | 3% |
| | Total | 70 | 100% |

By using the crosstabs function, the data were classified based on the vaccine types and racial classification. The results of data processing were shown that the Astra Zeneca vaccine was used by 5 Caucasian/White respondents, 10 Asian respondents, and 1 respondent of another race. Meanwhile, the Pfizer-BioNTech vaccine was used by 5 Caucasian/White respondents, 12 Asian respondents, 1 Black or African American respondent, and 7 respondents of other races. On the other hand, Sinopharm/Sinovac vaccine was used by 4 Caucasian/White respondents and 4 respondents of Asian race. As for the Moderna vaccine, 3 respondents were Caucasian/White, and 8 respondents were Asian. In contrast the Sputnik vaccine was used by 1 Caucasian/White respondent, 1 respondent of Asian race, and 3 respondents of other races. Then the last type of vaccine is Janssen (Johnson & Johnson), which was used by 1 Caucasian/White respondent, 2 respondents of Asian race, and 2 Black or African American respondents (Table 4).

### 4.2 Analysis of Adverse Events Following Covid-19 Vaccination Based on Naranjo Algorithm Method

Caucasian/White, Asian, Black or African American, and Other Races were the categories used in this study to categorize causality assessment interpretation depending on race and ethnicity. According to the questionnaire results, 42.1% of Caucasian/White respondents classified causality assessment as probable, which means the adverse event (1) demonstrated a reasonable time-related continuity after vaccine application, (2)

**Table 4.** Brand names of the COVID-19 vaccine with Race and Ethnicity Crosstabulation

| Brand names of the COVID-19 vaccine which have been used * Race and Ethnicity Crosstabulation | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | Race and Ethnicity | | | | Total |
| | | | Caucasian/White | Asian | Black or African American | Other Race | |
| Brand names of the Covid-19 vaccine which have been used: | AstraZeneca | Count | 5 | 10 | 0 | 1 | 16 |
| | | % | 31.3% | 62.5% | 0.0% | 6.3% | 100.0% |
| | Pfizer-BioNTech | Count | 5 | 12 | 1 | 7 | 25 |
| | | % | 20.0% | 48.0% | 4.0% | 28.0% | 100.0% |
| | Sinopharm/Sinovac | Count | 4 | 4 | 0 | 0 | 8 |
| | | % | 50.0% | 50.0% | 0.0% | 0.0% | 100.0% |
| | Moderna | Count | 3 | 8 | 0 | 0 | 11 |
| | | % | 27.3% | 72.7% | 0.0% | 0.0% | 100.0% |
| | Sputnik | Count | 1 | 1 | 0 | 3 | 5 |
| | | % | 20.0% | 20.0% | 0.0% | 60.0% | 100.0% |
| | Janssen (Johnson & Johnson) | Count | 1 | 2 | 2 | 0 | 5 |
| | | % | 20.0% | 40.0% | 40.0% | 0.0% | 100.0% |
| Total | | Count | 19 | 37 | 3 | 11 | 70 |
| | | % | 27.1% | 52.9% | 4.3% | 15.7% | 100.0% |

demonstrated a recognized response to the suspected vaccine, (3) was confirmed by withdrawal but not by exposure to the vaccine application, and (4) could not be reasonably exposed by known characteristics of the patient's clinical condition. The adverse events were then classified as possible by 31.6% of Caucasian/White respondents, which means that they (1) showed a time-related continuity after vaccine application, (2) possibly exhibited a recognized pattern to the suspected vaccine, and (3) could be explained by the patient's disease traits. In contrast, 26.3% of Caucasian and White respondents fell into the "doubtful" category, which denotes that it is likely that the adverse event was caused by causes other than the vaccination. Based on the data above, it could be concluded that the majority of Caucasians/White were probable for the causality assessment interpretation for adverse events following COVID-19 vaccination (Table 5).

In Asian respondents, different results were obtained for causality assessment interpretation with the definite group. 18.9% of respondents were categorized as having definite reactions, which means the reaction (1) had a predictable temporal sequence after the vaccination or had a toxic vaccine level established in body fluids or tissues, (2) showed a recognizable response to the suspected vaccine, and (3) was confirmed by improvement after the vaccination was stopped and reappearance after the reexposure. As for the probable group, the percentage obtained was 29.7%. Then the percentage

**Table 5.** Race and Ethnicity with Causality Assessment Interpretation Crosstabulation

| Race and Ethnicity * Causality Assessment Interpretation Crosstabulation | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | Causality Assessment Interpretation | | | | Total |
| | | | Definite | Probable | Possible | Doubtful | |
| Race and Ethnicity | Caucasian/White | Count | 0 | 8 | 6 | 5 | 19 |
| | | % | 0.0% | 42.1% | 31.6% | 26.3% | 100.0% |
| | Asian | Count | 7 | 11 | 14 | 5 | 37 |
| | | % | 18.9% | 29.7% | 37.8% | 13.5% | 100.0% |
| | Black or African American | Count | 0 | 1 | 2 | 0 | 3 |
| | | % | 0.0% | 33.3% | 66.7% | 0.0% | 100.0% |
| | Other Race | Count | 1 | 1 | 7 | 2 | 11 |
| | | % | 9.1% | 9.1% | 63.6% | 18.2% | 100.0% |
| Total | | Count | 8 | 21 | 29 | 12 | 70 |
| | | % | 11.4% | 30.0% | 41.4% | 17.1% | 100.0% |

of possible groups were 37.8%. In doubtful group, the percentage of respondents were 13.5%. The doubtful group indicates that the reaction was most likely caused by factors other than the vaccine. As a result, it was possible to conclude that the majority of causality assessment results for adverse events following COVID-19 vaccination were for Asian respondents.

For the Black or African American, the percentage of causality assessment interpretation for the adverse events following COVID-19 vaccination was only in probable and possible groups. Where the percentage of 33.3% was in the probable group. Meanwhile, the possible group was 66.7%. From the data obtained, it could be described that the majority of causality assessment interpretation in Black or African Americans was the possible group. In other races, causality assessment interpretations classified as definite and probable were 9.1% each. While the group included as possible group was 63.6%. Then for the doubtful group was 18.2%. So, it could be concluded that the majority of causality assessment interpretation was in the possible group.

In subsequent causality assessment analysis, the results of questionnaire data were classified by entering the type of vaccine used by the respondents together with race and ethnicity into the Crosstabulation. In the Astra Zeneca vaccine type, the causality assessment interpretation results obtained for the probable group was 40% of Caucasian/White respondents. As for the possible group, 20% of respondents were Caucasian/White. Then for the doubtful group, 40% of respondents were Caucasian/White. Of the Asians who received the Astra Zeneca vaccine, 40% belonged to the definite group, while the probable group was 30%, and the possible group was 10%. Then, the doubtful group was 20%. In others race, 100% of them belonged to the doubtful group (Table 6).

**Table 6.** Astra Zeneca Vaccine, Race and Ethnicity, and Causality Assessment Interpretation Crosstabulation

| Race and Ethnicity * Causality Assessment Interpretation * Brand names of the COVID-19 vaccine which have been used - Crosstabulation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Brand names of the COVID-19 vaccine which have been used: | | | | Causality Assessment Interpretation | | | | Total |
| | | | | Definite | Probable | Possible | Doubtful | |
| AstraZeneca | Race and Ethnicity | Caucasian / White | Count | 0 | 2 | 1 | 2 | 5 |
| | | | % | 0.0% | 40.0% | 20.0% | 40.0% | 100.0% |
| | | Asian | Count | 4 | 3 | 1 | 2 | 10 |
| | | | % | 40.0% | 30.0% | 10.0% | 20.0% | 100.0% |
| | | Other Race | Count | 0 | 0 | 0 | 1 | 1 |
| | | | % | 0.0% | 0.0% | 0.0% | 100.0% | 100.0% |
| | Total | | Count | 4 | 5 | 2 | 5 | 16 |
| | | | % | 25.0% | 31.3% | 12.5% | 31.3% | 100.0% |

In the Pfizer-BioNTech vaccine, the causality assessment interpretation results gained for the probable group was 20% of Caucasian/White respondents. For the possible group, 60% of respondents were Caucasian/White. Then for the doubtful group, 20% of respondents were Caucasian/White (Table 7).

Of Asian respondents who received the Pfizer-BioNTech vaccine, 50% were included in the probable group, while for the possible group, it was 50%. While in Black or African American with the Pfizer-BioNTech vaccine, for the possible group, the percentage was100%.

For the other race with the Pfizer-BioNTech vaccine, the definite group was 14.3%. The probable group was 14.3%. The possible group was 57.1%, and 14.3% belonged to the doubtful group (Table 8).

In Sinopharm/Sinovac vaccine, the causality assessment interpretation results for the probable group were 75% of the Caucasian/White respondents. The possible group, the percentage was 25% of respondents.

For Asian respondents who received the Sinopharm/Sinovac vaccine, the definite group was 25%. As for the possible group was 50% of the respondents. Then for the doubtful group was 25%.

In the Moderna vaccine, the causality assessment interpretation results for the probable group were 66.7% of Caucasian/White respondents. As for the possible group was 33.3%.

**Table 7.** Pfizer-BioNTech Vaccine, Race and Ethnicity, and Causality Assessment Interpretation Crosstabulation

| Race and Ethnicity * Causality Assessment Interpretation * Brand names of the Covid-19 vaccine which have been used - Crosstabulation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Brand names of the Covid-19 vaccine which have been used: | | | | Causality Assessment Interpretation | | | | Total |
| | | | | Definite | Probable | Possible | Doubtful | |
| Pfizer-BioNTech | Race and Ethnicity | Caucasian / White | Count | 0 | 1 | 3 | 1 | 5 |
| | | | % | 0.0% | 20.0% | 60.0% | 20.0% | 100.0% |
| | | Asian | Count | 0 | 6 | 6 | 0 | 12 |
| | | | % | 0.0% | 50.0% | 50.0% | 0.0% | 100.0% |
| | | Black or African American | Count | 0 | 0 | 1 | 0 | 1 |
| | | | % | 0.0% | 0.0% | 100.0% | 0.0% | 100.0% |
| | | Other Race | Count | 1 | 1 | 4 | 1 | 7 |
| | | | % | 14.3% | 14.3% | 57.1% | 14.3% | 100.0% |
| | Total | | Count | 1 | 8 | 14 | 2 | 25 |
| | | | % | 4.0% | 32.0% | 56.0% | 8.0% | 100.0% |

**Table 8.** Sinopharm / Sinovac Vaccine, Race and Ethnicity, and Causality Assessment Interpretation Crosstabulation

| Race and Ethnicity * Causality Assessment Interpretation * Brand names of the COVID-19 vaccine which have been used - Crosstabulation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Brand names of the COVID-19 vaccine which have been used: | | | | Causality Assessment Interpretation | | | | Total |
| | | | | Definite | Probable | Possible | Doubtful | |
| Sinopharm / Sinovac | Race and Ethnicity | Caucasian / White | Count | 0 | 3 | 1 | 0 | 4 |
| | | | % | 0.0% | 75.0% | 25.0% | 0.0% | 100.0% |
| | | Asian | Count | 1 | 0 | 2 | 1 | 4 |
| | | | % | 25.0% | 0.0% | 50.0% | 25.0% | 100.0% |
| | Total | | Count | 1 | 3 | 3 | 1 | 8 |
| | | | % | 12.5% | 37.5% | 37.5% | 12.5% | 100.0% |
| | | | % | 11.4% | 30.0% | 41.4% | 17.1% | 100.0% |

For Asians who received the Moderna vaccine, the definite group was 25%. The probable group was 25% of respondents. Then, the possible group was 37,5% of respondents. While the doubtful group, the percentage was 12,5% (Table 9).

Of Caucasians/White respondents who received the Sputnik vaccine, the doubtful group was 100%. Of the Asian race who received the Sputnik vaccine, 100% was

**Table 9.** Moderna Vaccine, Race and Ethnicity, and Causality Assessment Interpretation Crosstabulation

| Race and Ethnicity * Causality Assessment Interpretation * Brand names of the COVID-19 vaccine which have been used - Crosstabulation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Brand names of the COVID-19 vaccine which have been used: | | | | Causality Assessment Interpretation | | | | Total |
| | | | | Definite | Probable | Possible | Doubtful | |
| Moderna | Race and Ethnicity | Caucasian / White | Count | 0 | 2 | 1 | 0 | 3 |
| | | | % | 0.0% | 66.7% | 33.3% | 0.0% | 100.0% |
| | | Asian | Count | 2 | 2 | 3 | 1 | 8 |
| | | | % | 25.0% | 25.0% | 37.5% | 12.5% | 100.0% |
| | Total | | Count | 2 | 4 | 4 | 1 | 11 |
| | | | % | 18.2% | 36.4% | 36.4% | 9.1% | 100.0% |

included in the possible group. In the other race, 100% were included in the possible class (Table 10).

For the Janssen (Johnson & Johnson) vaccine, the causality assessment interpretation results were obtained for the doubtful group. 100% of respondents were Caucasian/White. Of Asian respondents, 50% were included in the possible group, while

**Table 10.** Sputnik Vaccine, Race and Ethnicity, and Causality Assessment Interpretation Crosstabulation

| Race and Ethnicity * Causality Assessment Interpretation * Brand names of the COVID-19 vaccine which have been used - Crosstabulation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Brand names of the COVID-19 vaccine which have been used: | | | | Causality Assessment Interpretation | | | | Total |
| | | | | Definite | Probable | Possible | Doubtful | |
| Sputnik | Race and Ethnicity | Caucasian / White | Count | | | 0 | 1 | 1 |
| | | | % | | | 0.0% | 100.0% | 100.0% |
| | | Asian | Count | | | 1 | 0 | 1 |
| | | | % | | | 100.0% | 0.0% | 100.0% |
| | | Other Race | Count | | | 3 | 0 | 3 |
| | | | % | | | 100.0% | 0.0% | 100.0% |
| | Total | | Count | | | 4 | 1 | 5 |
| | | | % | | | 80.0% | 20.0% | 100.0% |

**Table 11.** Janssen (Johnson & Johnson) Vaccine, Race and Ethnicity and Causality Assessment Interpretation Crosstabulation

| Race and Ethnicity * Causality Assessment Interpretation * Brand names of the COVID-19 vaccine which have been used - Crosstabulation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Brand names of the COVID-19 vaccine which have been used: | | | | Causality Assessment Interpretation | | | | Total |
| | | | | Definite | Probable | Possible | Doubtful | |
| Janssen (Johnson & Johnson) | Race and Ethnicity | Caucasian / White | Count | | 0 | 0 | 1 | 1 |
| | | | % | | 0.0% | 0.0% | 100.0% | 100.0% |
| | | Asian | Count | | 0 | 1 | 1 | 2 |
| | | | % | | 0.0% | 50.0% | 50.0% | 100.0% |
| | | Black or African American | Count | | 1 | 1 | 0 | 2 |
| | | | % | | 50.0% | 50.0% | 0.0% | 100.0% |
| | Total | | Count | | 1 | 2 | 2 | 5 |
| | | | % | | 20.0% | 40.0% | 40.0% | 100.0% |

50% for the doubtful group. In Black or African Americans with the Janssen (Johnson & Johnson) vaccine, the percentage of the probable and possible group were 50%, respectively (Table 11).

## 5 Conclusion

For all four types of racial classification, most causality assessments of adverse events following COVID-19 vaccination were in the "Probable" (30.0%) and "Possible" (41.4%) groups. In the "Probable" group, the percentage of the Caucasian/White race was 42.1%, the Asian was 29.7%, the Black or African American was 33.3%, and the other race was 9.1%. In contrast, in the "Possible" group, the Caucasian/White, Asian, Black, or African American, and other races were 31.6%, 37.8%, 66.7%, and 63.6%, respectively.

The definition of the "Probable" group states that the adverse events met the following criteria: (1) they demonstrated a reasonable time-related continuity after vaccination; (2) they demonstrated a recognized response to the suspected vaccine; (3) they were confirmed by withdrawal but not by exposure to vaccination; and (4) they could not reasonably have been caused by known clinical characteristics of the patient. The "Possible" category denotes that the adverse events (1) show a time-related continuity after vaccination, (2) may display a pattern that is known to be associated with the suspected vaccine, and (3) may be accounted for by the characteristics of the patient's disease.

**Limitation**

One of the study's limitations is the small sample size of 70 respondents, which still exceeds the sample size in one of the reference journals [19]. Furthermore, using only

one type of method may be deemed insufficient, so researchers intend to compare the Naranjo algorithm with the World Health Organization's Causality Assessment of an Adverse Event Following Immunization in future studies (WHO) [17].

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**Availability of Data and Material.** The corresponding author will provide the datasets produced and/or analyzed during the current work upon reasonable request.

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**Ethical Consideration** The questionnaire respondents were voluntary participants who were free to choose to participate without any pressure or coercion.

**Declaration.** The authors certify that none of their known competing interests appeared to have an impact on the research presented in this study.

**Conflict of Interest.** There are no potential conflicts of interest regarding the research, authorship, or publication of this article, according to the author(s).

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| 2 | Anggota | 10 Jam x 2 | Rp 50.000,00 | Rp 100.000,00 |
| 3 | Pembantu Teknis Lapangan | 6 jam x 2 | Rp 40.000,00 | Rp 80.000,00 |
| **Jumlah Biaya** | | | | **Rp 300.000,00** |

2 Bahan Habis Pakai dan Peralatan

| No | Bahan | Volume | Biaya Satuan | Biaya |
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| 2 | Tinta Refill Printer HP 360 | 2 buah | Rp 180.000,00 | Rp 360.000,00 |
| 3 | Alat Tulis | 4 Pack | Rp 50.000,00 | Rp 200.000,00 |
| 4 | Materai | 34 buah | Rp 10.000,00 | Rp 340.000,00 |
| 5 | Buku Pedoman | 20 bh | Rp 35.000,00 | Rp 700.000,00 |
| 6 | Biaya Paket Pulsa | 52 | Rp 50.000,00 | Rp 2.600.000,00 |
| **Jumlah Biaya** | | | | **Rp 4.400.000,00** |

3 Rincian Pengumpulan dan Pengolahan Data, Laporan, Publikasi Seminar dan Lain-lain

| No | Komponen | Volume | Biaya Satuan | Jumlah |
|---|---|---|---|---|
| 1 | Pengumpulan dan Pengolahan Data | 1 | Rp 500.000,00 | Rp 500.000,00 |
| 2 | Penyusunan Laporan | 3 | Rp 150.000,00 | Rp 450.000,00 |
| 3 | Desiminasi/ Seminar | 1 | Rp 300.000,00 | Rp 300.000,00 |
| 4 | Publikasi / jurnal | 1 | Rp 800.000,00 | Rp 800.000,00 |
| **Jumlah Biaya** | | | | **Rp 2.050.000,00** |

4 Perjalanan

| Material | Tujuan | Kuantitas | Jumlah |
|---|---|---|---|
| Ketua | a. Pengorganisasian Persiapan Kegiatan<br>b. Pendampingan Pendidikan dari UMSurabaya<br>c. Evaluasi Kegiatan, dll | 100 kali | Rp 2.500.000,00 |
| Anggota | a. Pengorganisasian Persiapan Kegiatan<br>b. Pendampingan Pendidikan dari UMSurabaya<br>c. Evaluasi Kegiatan, dll | 50 kali | Rp 1.500.000,00 |
| **SUB TOTAL** | | | **Rp 4.000.000,00** |

**TOTAL KESELURUHAN** **Rp 10.750.000,00**

# SURAT TUGAS

**Nomor: 94/TGS/II.3.AU/LPPM/F/2021**

***Assalaamu'alaikum Wr. Wb.***

Yang bertandatangan di bawah ini:

Nama : Dede Nasrullah, S.Kep., Ns., M.Kep
Jabatan : Kepala LPPM
Unit Kerja : LPPM Universitas Muhammadiyah Surabaya

Dengan ini menugaskan:

| No | Nama | NIDN/NIM | Jabatan |
|---|---|---|---|
| 1. | Apt. Rachma Dessidianti, S.Farm, M.Sc | - | Dosen UMSurabaya |
| 2. | Malika Ilma Alkautsar | 20201666017 | Mahasiswa UMSurabaya |
| 3. | Nabila Mirza Azizi | 20201666030 | Mahasiswa UMSurabaya |

Untuk melaksanakan Penelitian kepada masyarakat dengan judul "Casuality Assesment of Adverse Event For Covid Vaccine In Compare Between Racial Classification Using Naranjo Algorithm". Penelitian ini dilaksanakan di Program Studi S1 Farmasi Fakultas Ilmu Kesehatan UMSurabaya pada tahun akademik 2021-2022.

Demikian surat tugas ini, harap menjadikan periksa dan dapat dilaksanakan dengan penuh tanggung jawab.

***Wassalaamu'alaikum Wr. Wb***

Surabaya, 27 Agustus 2021
LPPM UMSurabaya

Dede Nasrullah, S.Kep., Ns., M.Kep
NIP. 012.05.1.1987.14.113



ADDRESS
Jl. Sutorejo No. 59 Kota Surabaya
Provinsi Jawa Timur Indonesia 60113
www.um-surabaya.ac.id

CONTACT
Phone : 031 3811966
Fax : 031 3813096
Email : rektorat@um-surabaya.ac.id

**Surat Kontrak Penelitian Internal**
**LEMBAGA PENELITIAN DAN PENELITIAN KEPADA MASYARAKAT (LPPM)**
**UNIVERSITAS MUHAMMADIYAH SURABAYA**
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Pada hari ini **Jumat** tanggal **Dua Puluh Tujuh** bulan **Agustus** tahun **Dua Ribu Dua Puluh Satu**, kami yang bertandatangan dibawah ini :

1. Dede Nasrullah, S.Kep., Ns., M.Kep. : Kepala LPPM UMSurabaya yang bertindak atas nama Rektor UMSurabaya dalam surat perjanjian ini disebut sebagai **PIHAK PERTAMA**;
2. Apt. Rachma Dessidianti, S.Farm, M.Sc : Dosen UM Surabaya, yang selanjutnya disebut **PIHAK KEDUA**.

untuk bersepakat dalam pendanaan dan pelaksanaan program penelitian:

Judul : Casuality Assesment of Adverse Event For Covid Vaccine In Compare Between Racial Classification Using Naranjo Algorithm

Anggota : Malika Ilma Alkautsar, Nabila Mirza Azizi

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ADDRESS
Jl. Sutorejo No. 59 Kota Surabaya
Provinsi Jawa Timur Indonesia 60113
www.um-surabaya.ac.id
CONTACT
Phone : 031 3811966
Fax : 031 3813096
Email : rektorat@um-surabaya.ac.id

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ma

Dede Nasrullah, S.Kep., Ns., M.Kep
NIK. 012.05.1.1987.14.113

Pihak Kedua

Apt. Rachma Dessidianti, S.Farm, M.Sc



ADDRESS
Jl. Sutorejo No. 59 Kota Surabaya
Provinsi Jawa Timur Indonesia 60113
www.um-surabaya.ac.id

CONTACT
Phone : 031 3811966
Fax : 031 3813096
Email : rektorat@um-surabaya.ac.id

# KUITANSI

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Bendahara LPPM,
Universitas Muhammadiyah Surabaya

Holy Ichda Wahyuni

Ketua Penelitian

Apt. Rachma Dessidianti, S.Farm, M.Sc



ADDRESS
Jl. Sutorejo No. 59 Kota Surabaya
Provinsi Jawa Timur Indonesia 60113
www.um-surabaya.ac.id

CONTACT
Phone : 031 3811966
Fax : 031 3813096
Email : rektorat@um-surabaya.ac.id